A Dissertation on

A STUDY OF PROGNOSTIC PREDICTORS IN GUILLAIN-BARRE SYNDROME

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DECLARATION

DECLARATION

I solemnly declare that the dissertation titled **"A STUDY OF PROGNOSTIC PREDICTORS IN GUILLAIN-BARRE SYNDROME"** was done by me from JULY 2016 to JUNE 2017 under the guidance and supervision of Professor **Dr. KUMAR NATARAJAN M.D.,**

This dissertation is submitted to **The Tamilnadu Dr. M.G.R. Medical University** towards the partial fulfilment of the requirement for the award of MD Degree in General Medicine (Branch I).

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factors.Studies showing of HLA associations with GBS are generally not evident.[48][49]. Only few small number of familial cases of GBS have been described. [50][51] Although antiganglioside antibodies are the most commonly reported antibody in GBS there are other reports of antibodies that might be pathogenic in a small number of patients. Antibodies against a protein in the node of Ranvier "neurofascin" have received recent attention with serum of 4% of patients with AIDP being positive in one recent study [52] .

Neurophysiology is useful in the diagnosis and definition of the subtype of GBS. Early assessment in the course of the disease frequently shows small action potentials, prolonged distal motor latency, delayed F waves, and conduction block. [53] .Occasionally the study is normal for the first time and a repeated study is required to definitely document a peripheral nerve disorder. Axonal types of the illness are characterised by reduced motor and or sensory action potentials with denervation potentials once the acute stage of the disease is over. Neurophysiological studies carried out as part of the European Ivlg and steroid trial found 69% of the studies to be consistent with AIDP with only 3% suggesting axonal pathology on studies carried out within 3 weeks of onset ,twenty-three percent of studies were equivocal at this early stage and may have gone on to be predominantly axonal. [54] Classification of the variants of Guillian Barre Syndrome:

Acute inflammatory demyelinating polyneuropathy Acute motor sensory axonal neuropathy (AMSAN) Acute motor axonal neuropathy Miller fisher syndrome

Pure sensory forms Pure motor forms Absence of nystagmus or dysarthria with ataxia Severe motor sensory GBS GBS with severe bulbar & facial paralysis Acute pandysautonomia.

Clinical manifestations of GBS: 1) Stage of invasion 2) Progression & plateau phase 3) Stage of regression

Clinical Features and electrophysiological characteristics Clinically GBS is a monophasic disease typically characterised by ascending type of progressive and relatively symmetrical weakness of the lower and upper

LIST OF ABBREVIATIONS USED

- ANS- Autonomic nervous system
- CNS- Central nervous system
- EDX - Electrodiagnostic
- EAN - Experimental Allergic Neuritis
- PNS- Peripheral nervous system
- GBS-Guillain-Barre syndrome
- MFS-Miller Fisher Syndrome
- AIDP-Acute inflammatory demyelinating neuropathy
- AMAN-Acute Motor Axonal Neuropathy
- AMSAN-Acute Motor Sensory Axonal Neuropathy
- WHO-World health organisation
- AAN-American academy of Neurology
- IVIg-Intravenous Immunoglobulin
- CMAP-Compound Muscle Action Potential
- SNAP-Sensory nerve action potential
- PE-Plasma Exchange
- CSF-Cerebrospinal Fluid
- MRC SSS- Medical Research Council Sum Score Scale
- SD-Standard Deviation
- NCV-Nerve conduction velocity
- CMV-Cytomegalovirus

- EBV-Ebstein Barr Virus
- MIP-Maximum Inspiratory Pressure
- MEX-Maximum Expiratory Pressure
- FVC – Forced Vital Capacity

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INTRODUCTION

INTRODUCTION

Guillain-Barré syndrome (GBS) is “an acute immune-mediated acute polyradiculoneuropathy disorder”. The syndrome is named after the French physicians “Georges Guillain and Jean Alexandre Barre”, who described it in 1916. GBS is one of the commonest acquired peripheral nerve demyelinating disorder, its an acute, usually postinfectious neuropathy of common occurrence with a yearly incidence rate between 1.1 and 1.8 per 100 000[1]

GBS incidence increases exponentially with age, with age-specific rates increasing from 0.62 per 100 000 among 0-9-year-olds to 2.66 per 100 000 among 80-89-year-olds. Male subjects are more commonly affected with an RR of 1.78.[2].The most likely preceding infection is Campylobacter jejuni enteritis. Other preceding infectious agents include Mycoplasma pneumonia , Haemophilus influenza,Cytomegalovirus and Epstein Barr virus. As its typical presentation, GBS causes very rapidly progressing diffuse proximal and distal muscle weakness of the four limbs, sensory loss symptoms with are flexia. The maximal weakness is reached within duration of 4 weeks as given by definition. In majority of cases, nadir is attained within 2 weeks. Cranial nerve involvement with Facial, bulbar muscle palsy and weakness of respiratory muscle is frequent. Autonomic nerve involvement is very well described. GBS is best diagnosed clinically but it may be aided by electrophysiology .The two main electrophysiological subtypes acute inflammatory demyelinating polyradiculoneuropathy (AIDP), which is sensory and motor and displays demyelinating changes on nerve conduction studies, and acute motor axonal neuropathy (AMAN), which is primarily axonal and thought to be purely motor. There are also axonal pathology with sensory involvement described as acute motor and sensory axonal neuropathy (AMSAN). Very recently, it has been shown that the pathophysiology of axonal subtypes is characterised besides axonal degeneration by reversible conduction failure and it is shown that AMAN and AMSAN which has unique immunological profile and electrophysiological study features ,can represent a continuity in the axonal types of GBS spectrum. Elevated cerebrospinal fluid (CSF) protein level with normal CSF cellularity, also known as 'albumino-cytological dissociation',is present in over 90% of patients within 2 weeks of onset is characteristic of GBS. Radio imaging is also contributory to the diagnosis of GBS, with MRI of the lumbar spine demonstrating thickened and/or enhancing nerve roots.[3&4] The prognosis of GBS is generally considered very favourable. Inspite of the demonstrated efficacy of intravenous immunoglobulins (IVIg) and plasma exchange, GBS still remains a disabling disease in a significant proportion of patients.These treatments have not improved mortality. Long-term improving function is compromised in a significant proportion of patients. Prognosis of the disease and potential predictors of clinical outcome in the illness have been studied in Coimbatore medical college Hospital.

AIMS & OBJECTIVES

AIMS

- To study the prognostic predictors in Guillain-Barre Syndrome for the functional outcome.

OBJECTIVES

- To assess the various predictors like Age, MRC score at the time of admission, Bulbar palsy, autonomic dysfunction, neck flexor weakness, axonal variety on electrophysiological assessment, requirement of ventilator assistance, associated with the disease for the functional outcome of the disease.
- To assess the patients at regular intervals throughout the course of the disease from the time of admission till discharge with Hughes motor scale.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

History of Guillian Barre Syndrome

In 1843 Robert graves identified pathology of the disease was causing paralysis involving the peripheral nerve. Jean baptiste octave laundry in 1859 identified that the disease causing paralysis not involving central lesions, might be due to involvement of peripheral nerve. The pathologic involvement of disease process was demonstrated first by Dumenil in rouen in 1864.The term acute febrile polyneuritis was first to be coined by osler. In 1916 Georges Guillain Andrew S trohl, Jean Alexander Barre demonstrated in two French soldiers involving peripheral nerves. They also studied the CSF that increased protein in CSF with absence of cells .In 1969 Asbury ,Adams, Amason ,explained the similarities between experimental allergic neuritis in animals and GBS.

GBS is an immunologically mediated demyelinating disorder involving peripheral nerve clinically charecterised by acute onset of symmetrical progressive muscle weakness with loss of myotatic reflexes (Asbury.cornblath.1990).

Etiology

From the studies its shown that almost 50-70% of cases of GBS have been associated with an antecedent infection or vaccination with an interval of 1-4 weeks. Although many infectious agents leads to the pathogenesis of GBS, idiopathic etiological manifestation of certain cases is found in 25- 30% of population.

Pathophysiology of GBS

Autopsy studies are rare in GBS because very less patients die. Earlier studies showed edema of the peripheral nerves only with little inflammatory infiltrate.[5] Classic studies previously by" Asbury and colleagues" shows the importance of perivascular lymphocytes which simulated the findings in the classic animal model experimental allergic neuritis.[6] They postulated an definite immunological basis for the peripheral nerve system demyelination involving with lymphocytes which had influenced the cause of GBS. Macrophage associated demyelination have been found in the Electron microscopic studies of nerve biopsy. Macrophages shows appearance of invading the Schwann cell basement membrane and phagocytose myelin debris.[6][7] Pathological studies of AMSAN and AMAN show a relative paucity of inflammatory infiltrate with axonal destruction but this time macrophages were situated between the myelin and axons especially in the region of the node of Ranvier.[8] .In pathological studies of GBS, it suggest that the macrophage is the key element of nerve damage but may well be targeted to either the myelin or axon by antibodies. In AMSAN type of GBS pathological changes are similar but involve both motor and ventral nerve roots.[9].

The major pathophysiological process involved in GBS is either demyelination only or with primary axonal damage. There is found a molecular mimicry between the glycans on lipo-oligosaccharides of the antecedent infectious agents and the ganglioside on the myelin sheath resulting in formation of various antigangliosides antibodies. These antibodies play an important role in demyelination and axonal injury.[10][11]. The various antiganglioside antibodies seen in GBS patients include GM-1,GM-2,GM-3,GD-1a,GT-1b,GQ-1b.[11][12]. Of these GM-1 GD-1a has been significantly associated with AMAN, type 25 GM-3 with Acute inflammatory Demyelinating Polyneuropathy(AIDP) ,GQIb-Miller Fisher Syndrome(MFS) and GT-1b with bulbar palsy in GBS patients. 25GM-1 has good correlation with disease activity .[10]

Immunology

The recognition that there was an association between GBS and a variety of triggering infections strongly suggested that there must be an immunological cause for the syndrome. This was supported by the nature of the pathological changes with macrophage targeted, demyelination in at least AIDP which could be used to support an antibody mediated disorder. The efficacy of plasma exchange in shortening the time taken to recover also argued for a serum factor mediating the disease. In the 1960's Melnick [13] was one of the first to publish data suggesting complement fixing antibodies in the acute phase of GBS. These studies were difficult to replicate but sensitive C1 esterase assays supported complement consumption and a role for complement in the disorder [14]. In rabbits immunisation with galactocerebroside can produce a demyelinating neuropathy, suggesting that antibodies against myelin antigens are capable of causing neuropathy.[15].The pathology of the human disease resembled the experimental model experimental allergic neuritis produced by immunising susceptible species with peripheral nerve in adjuvant. EAN can be elicited using individual proteins from myelin such as P0 and P2 and T cell lines reacting with P2 can transfer the disease. [16][17] This stimulated numerous studies attempting to find antibodies to P2, P0, and other protein antigens in GBS but these were largely negative.[18]. Antibodies recognising lipids were identified in the 1980's and increasingly recognised in certain subgroups of GBS.[19]. The identification of antibodies against one of these gangliosides, GQ1b in 95% of patients with Miller Fisher Syndrome.[20][21]supported a role for such antibodies in the pathogenesis of this syndrome thought to be very closely related to GBS. Similar antibodies were also found in GBS with ophthalmoplegia and in Bickerstaff 's encephalitis.[22][23] In vitro studies of mouse hemidiaphragm preparations showed that antiGq1b monoclonals immunostained the neuromuscular junction where they fixed complement and bound in identical ways to patient serum.[24] Antiganglioside antibodies were found to be associated with AMAN [25] and were implicated in animal models of the disease in rabbits [26]. Furthermore, patients immunised with gangliosides [27] were known to develop neuropathies in certain circumstances adding to the body of evidence supporting a pathology for GBS which involved complement fixing antibodies against human gangliosides. Although the evidence in support of antiganglioside antibodies as a cause of MFS and AMAN was strong the most common form of GBS on Western countries (AIDP) was only rarely associated with ganglioside antibodies using conventional techniques [28]. The frequency of antiganglioside antibodies increases if antibodies against complexes of more than one ganglioside are considered although there are as yet few published studies .[29] [30]Antibodies against gangliosides are usually found to be of the type IgG1 or IgG3 subtype that conventionally require T lymphocyte cell help in their production. T lymphocyte cells can infiltrate the pathological lesion in peripheral nerve therefore it seems likely that they play a important part in mediating antibody production. Many studies have found raised concentrations of activated T lymphocte cells in the peripheral blood among patients with GBS [31] as well as changes in regulatory T cells [32] and raised levels of T cell derived cytokines.[33] The previous studies looking at T cell reactivity against protein antigens such as the P2 Protein which were causing in EAN wasproved to be more negative. Yδ T cells which are capable of recognising nonprotein antigens such as gangliosides have been isolated from GBS involving peripheral nerve but may also be isolated from patients with vasculitis.[34] There is possible evidence that even T cells may be playing a important role but lack of strong evidence is found. Yδ T cells are restricted by CD1 which is upregulated in nerve from patients with GBS [35] but no clear CD1 polymorphism is linked to GBS.[36] GBS clinical features are always found to be variable and several attempts have been made to correlate this with the distribution of gangliosides in different nerves.[37] There is more GQ1b in the ocular nerves which might explain the ophthalmoplegia in Miller Fisher syndrome. Similarly ventral nerve roots contain more GM1 than dorsal roots.

The actual densities and accessibilities of the gangliosides in different tissues may be more important and there are studies suggesting that access to gangliosides by antibodies may differ [38].

C. jejuni is the best studied triggering agent for GBS and has been shown to have ganglioside like structures in the lipopolysaccharide coat of the bacterium [39][40]. Similar examples of molecular mimicry are seen with other organisms that trigger GBS such as Haemophilus [41] and Cytomegalovirus [42]. Therefore it seems plausible to hypothesise that antecedent infection with one of these infectious agents leads to antibody production which cross-reacts with gangliosides and other glycolipids leading to myelin particle destruction. This could occur by complement activation or by antibodies targeting macrophages via the fc receptor and leading to both conduction failure and demyelination. Therefore to mediate disease such specific antibodies need to pass through the blood nerve barrier. Studies in EAN suggest that activated T cells may open up the barrier to allow the antineural antibodies to mediate nerve damage.[43][44]. Of course it is possible that breakdown in the blood nerve barrier is a nonspecific event that allows antigen specific antibodies to penetrate and mediate disease. Matrix metalloproteinases have been implicated in mediating barrier breakdown [45]. There may be specific factors about the triggering infection that increase the likelihood of immune sensitivity to a specific agent. Certain serotypes of C. jejuni appear more likely to produce these autoreactive antibodies perhaps by containing more neuritogenic epitopes.[46][47]. The risk of GBS after C. jejuni enteritis is estimated to be about 1 in 1000. This risk is mostly by triggeredby immunological genetic factors. Studies showing of HLA associations with GBS are generally not evident.[48][49]. Only few small number of familial cases of GBS have been described.[50][51] Although antiganglioside antibodies are the most commonly reported antibody in GBS there are other reports of antibodies that might be pathogenic in a small number of patients. Antibodies against a protein in the node of Ranvier "neurofascin" have received recent attention with serum of 4% of patients with AIDP being positive in one recent study [52].

Neurophysiology is useful in the diagnosis and definition of the subtype of GBS. Early assessment in the course of the disease frequently shows small action potentials, prolonged distal motor latency, delayed F waves, and conduction block.[53].Occasionally the study is normal for the first time and a repeated study is required to definitely document a peripheral nerve disorder. Axonal types of the illness are characterised by reduced motor and or sensory action potentials with denervation potentials once the acute stage of the disease is over. Neurophysiological studies carried out as part of the European IvIg and steroid trial found 69% of the studies to be consistent with AIDP with only 3% suggesting axonal pathology on studies carried out within 3 weeks of onset ,twenty-three percent of studies were equivocal at this early stage and may have gone on to be predominantly axonal. [54]

Classification of the variants of Guillian Barre Syndrome

- Acute inflammatory demyelinating polyneuropathy
- Acute motor sensory axonal neuropathy(AMSAN)
- Acute motor axonal neuropathy
- Miller fisher syndrome
- Pure sensory forms
- Pure motor forms
- Absence of nystagmus or dysarthria with ataxia
- Severe motor sensory GBS
- GBS with severe bulbar & facial paralysis
- Acute pandysautonomia.

Clinical manifestations of GBS

1) Stage of invasion
2) Progression & plateau phase
3) Stage of regression

Clinical Features and electrophysiological characteristics

Clinically GBS is a monophasic disease typically characterised by ascending type of progressive and relatively symmetrical weakness of the lower and upper limbs associated with generalised areflexia or hyporeflexia.[55] Clinical features usually progress for 2-4 weeks reaches a nadir and enters a plateau phase[56].The weakness in GBS is most commonly ascending type of paralysis with intial involvement of ankle dorsi flexors, hip and knee flexors,ascending to involve abduction of shoulder and extension of elbow. Sensory symptoms including proximal limb pain is a common intial presentation though objective sensory signs are rare.[57]Cranial nerve involvement most likely bilateral facial nerve palsy is common. Autonomic disturbance such as orthostatic hypotension, resting tachycardia can be seen. CSF analysis in some of these patients show albuminocytological dissociation elevation protein levels in the absence of pleocytosis.[59] This is found in only 50% of Asian patients. [59] Respiratory failure with requirement of mechanical ventillatory support is seen in 20-30% of patients especially during the progressive phase of disease.[56]

Based on the nerve conduction study (NCS) results, the classic types of GBS are Acute Inflammatory Deyelinating Polyradiculopathy (AIDP), Acute Motor Axonal Neuropathy (AMAN) and Acute Motor Sensory Axonal Neuropathy (AMSAN). AIDP is the most common type with better prognosis when compared to the axonal types (AMAN and AMSAN). Other rare variants include Miller Fisher syndrome (MFS),pure motor, ataxic GBS, pharyngocervicobrachial and pandysautonomia.[61].NCS results are best when done during the second week of illness. NCS patterns include (a) demyelination (AIDP)-Prolonged distal latencies, reduced NCV ,prolonged F wave latency, conduction block and temporary dispersion ,and (b) axonal forms (AMAN and AMSAN) characterized by decreased motor and sensory action potential amplitude. [62]Frequency of occurence of demyelinating type of GBS in about 90% in European and north American countries , whereas in Asian countries like China and Japan the major type in axonal forms is seen in 30-60% of cases. [61][62]. Further Indian studies are needed to delineate electrophysiological patterns that predominate in various age groups, regions and income level. [61]

Sensory symptoms usually mark the onset of the illness followed by sudden rapidly progressive distal muscle weakness that soon spreads proximally. Lumbar pain may be common and it represents inflammation in the nerve roots and may coincide with the breakdown in the nerve CSF barrier that allows protein to leak into the CSF. The weakness present in GBS is typically of “pyramidal in distribution” with ankle dorsiflexion, knee flexion and hip flexion very often severely involved and similarly the weakness in the arms is usually more severe in abduction of shoulder and extension of elbow . While sensory symptoms are common sensory signs are usually minor and may be limited to loss of vibration and proprioception. The significance of decreased or absent reflexes with no objective loss of large sensory fibres and finally yet complete paralysis will leads to a frequent misdiagnosis of hysteria.

The involvement of respiratory muscles may be sudden and unexpected but usually the vital capacity falls steadily and intubation of patient with ventilator support are required at level of approximately 1 litre.[68]

Autoimmune Diseases as papilloedema.[69] thought to be due to secondary causes as cerebral oedema and hyponatraemia.[70]. Mild autonomic disturbance is seen in three quarters of patients but a few develop severe bradyarrhythmias which are recognised as a cause of infrequent death from the syndrome.

Mortality in most population studies is between 5 and 10 percent .[71]. The disease is monophasic with weakness reaching its most severity in 4 weeks followed by a plateau phase and then recovery. 60% of patients are able to walk unaided by 12 months [72] and the rest are left with various degrees of residual symptoms.

In three quarters patients, a history of a preceding illness usually respiratory or gastrointestinal which may be so mild as to be completely asymptomatic. The neuropathy classically begins 7–10 days after such triggering infection.Many other numerous antecedent events are described including surgery and immunisation. Most recent epidemiological surveys show the risk of immunisation triggering GBS to be very low [73]. It is estimated that the risk of contracting GBS from current influenza vaccines is significantly lower than the risk of getting GBS from influenza itself. Serological studies done have shown that Campylobacter jejuni, Epstein barr virus, and Cytomegalovirus are the most frequent antecedent infections.

Patients sometimes may continue to secrete C jejuni in their stool for up to 3 months following the onset of GBS[74].Persistent infection with CMV, EBV is very rare. A number of reports associate GBS with Mycoplasma pneumonia, influenza, and varicella [75].

Management

Management of GBS included supportive and immunological treatment – Plasma Exchange (PE) and intravenous immunoglobulin (IVIg). PE is a technique which consists of separation of plasma by two techiniques – membrane filtration and centrifugation, followed by infusion of blood cells back into the patient.[76]. It has been shown that there is significant improvement in disability when given within 4 weeks of illness as compared to supportive treatment alone.[77] .IVIg is obtained from purified human plasma pool from many donors. The possible mechanisim by which it acts include antibody attack on Schwann Cell membrane ,myelin, axolemma by blocking FcR on macrophages ,presence of anti-idiotypic antibodies that regulates autoantibodies, modulation of cytokines production, regulatory effects on B-cells and T cells .[78][79] . Both Plasmapheresis and IVIg have equal efficacy in hastening recovery in GBS.[80] [81] [82].The major adverse events seen in Plasmapheresis include hemodynamic instability, pneumonia, atelectasis, central venous access related complications and technical support and those with IVIg include anaphylaxsis reactions especially in IgA deficient individuals, transaminitis, pancytopenia, headache, thromboembolic events [81]. There is no significant difference in adverse events between the two modalities except that higher rates of complication are seen with Plasmapheresis as compared to IVIg .[80]

Patients with clinical symptoms of GBS but are capable to walk unaided for more than 5 metre and also who are clinically stable can be managed conservatively at peripheral centers. Those patients should be observed for progression of the disease, even if they are still within the first week of the onset of the disease. Blood pressure along with heart rate fluctuations, clinical signs with impending respiratory failure should be carefully observed and meticulously monitored. Clinically signs of paralytic ileus should be monitered. If any impending signs are detected they should be immediately shifted to higher specialized centers for further expert management. During acute phase of illness with bed-bound adult patients require both immunetherapy and supportive treatment. Immunetherapy should be used only after taking into the cost factors and the clinical status of the illness staging, other comorbid conditions and also complications of individual patients.

Supportive care

Immunotherapy is not the only modality to reduce the mortality in GBS. Mortality is due to disease-related issues or secondary complications developed in hospital due to prolonged disease course. Meticulous and attentive care of these patients are essential in reducing the mortality, supportive care guidelines and consensus guidelines have been published.[83]

Respiratory failure

GBS is one of the most common peripheral neuropathy causing respiratory difficulty and paralysis. Despite recent advances in respiratory distress management along with immunotherapy, mortality from GBS is very high as 20% for ventilated patients, Mechanical ventilation is usually required by one third of the patients. [83] Clinical signs such as tachypnea, asynchronous movements of chest and abdomen ,tachycardia, brow sweating and a vital capacity < 20 mL/kg,maximal expiratory pressure < 40 cm H_2O, maximal inspiratory pressures < 30 mm H_2O, predicts surely imminent respiratory failure.[83] Time from the onset of symptoms to admission of less than 1 week, facial weakness, neck weakness, bulbar paresis, and are other factors associated with respiratory failure.[83][84][85]Simple bedside test like single breath count, which correlates lung functions test well with vital capacity than phrenic nerve electro conduction studies is a good predictor of respiratory failure (Unpublished data by Meena *et al* from NIMS, Hyderabad). Percutaneous dilatational tracheostomy procedure may be advantageous over traditional tracheostomy procedure by permitting less risk of accidental extubation and a better appearing cosmetic outcome. Normally it takes 2–6 weeks to wean out of ventilatory support.[86] Tracheostomy procedure may be performed 2 weeks following intubation and should be based on respiratory status of an individual. It provides comfortness and airway safety but is associated at times with life-threatening complications and disfiguration.[83] If pulmonary function is improving, it may be preferable to wait for 1 more week to attempt at weaning off from ventilator.

Management of Dysautonomia

Almost 20% of GBS patients might have symptoms of dysautonomia like orthostatic hypotension, labile hypertension, sinustachycardia, arrythmias or sinus arrest. This rate increases upto 75% in patients with tetraplegia. Proprioceptive loss in patients predicts dysautonomia independently from the severity of weakness. It is most frequently responsible for dysautonomia. The afferent limb of cardiovascular regulation contains more myelinated fibers than the sympathetic and parasympathetic efferences, which determine the common classification of dysautonomia. The frequence of mixed sympathetic and parasympathetic hyperactivity is hard to explain by efferent lesions. Afferent conduction block releases the sympathetic efference of the baroreceptor reflex. The resulting catecholamine excess explains hypertension, tachycardia, ECG-changes and hyperglycemia. Norepinephrine sensitizes left ventricular stretch receptors. They induce cardiovascular depression and neurocardiogenic syncope which has a temporal behaviour similar to the blood pressure variations of GBS. Conduction block of sinoatrial stretch receptors causes inappropriate secretion of ADH and Renin. Dysbalance between myelinated and unmyelinated afferents which decrease and increase heart rate may cause parasympathetic hyperactivity, as exemplified by pulmonary stretch receptors that are stimulated by artificial ventilation. Wrong afferent feedback is responsible for many cardiovascular instabilities in GBS. Blockade of misguided efferent reactions is an attractive therapeutical approach.

Hyponatremia is one of the common electrolyte abnormality in GBS and is mainly due to SIADH in majority of the cases and natriuresis. The treatment pattern is different for both. Both requires replenishment of sodium, but SIADH needs fluid restriction and in case of natriuresis requires intravascular volume expansion. The best way to identify these two entities is by measuring central venous pressure.

Deep vein thrombosis prophylaxsis

All patients should be given subcutaneous fractionated or unfractionated heparin and support stockings until they are able to walk independently to prevent deep vein thrombosis .[83]If a prolonged bedridden period is anticipated and a tracheostomy has already been performed, institute oral anticoagulant treatment with Warfarin (Coumarin).

The Pain and sensory symptoms are found in majority of patients with GBS and should be treated effectively with opioid analogues. Sedation and decreased bowel motility may become a complication. Other drugs, such as gabapentin, carbamazepine acetaminophen, NSAIDs and tricyclic antidepressants also can be used.[169]

Nutrition

Nasogastric feeding should be administered early with slow in timing. High energy (40–45 nonprotein kcal) and high protein diet (2–2.5 g/kg) have been recommended to GBS patients so has to reduce muscle wasting and to assist respiratory weaning. Continuous enteral feeding seems to be better tolerated than bolus feeding in these patients.[169]

Surviellance for infections with weekly or more frequent sputum and urine cultures and blood count may be useful in early intervention but the use of it should be monitered by clinical circumstances.[169]

Immunotherapy

Both plasma exchange and IVIg are effective immunotherapies for adult and pediatric patients with GBS if given during the first few weeks of disease.

Plasmapheresis

Studying a meta-analysis of 6 class II trails comparing plasma exchange (PE) to supportive care alone for adults with GBS, it was found that PE reduced the risk of developing respiratory failure.[87][88]. Patients treated with PE fared significantly better in the following secondary outcome measures time to recover walking without aid, percentage of patients requiring artificial ventilation, duration of ventilation, full muscle strength recovery after 1 year, and severe sequelae after 1 year time to onset of motor recovery in mildly affected patients was significantly shortened in the PE group, however, the cost of PE has been shown to be offset by the savings of shorter hospital stay.[89]The volume of plasma removed and the optimum number of PE has not been established and it varies in different trials, but many physicians use the protocol of North American trial in which a total of 200–250 mL/kg was exchanged over 7–10 days all over the world.[90] . There is evidence that the number of PE in GBS should be adjusted to disease severity and that also patients with mild symptoms do benefit from PE.[91]

In mild GBS, two sessions of PE are superior to none, in moderate GBS, 4 sessions are superior to 2, in severe GBS, 6 sessions are no better than 4, in line with these findings, Yuki *et al* reported that at least 2 PE are needed to significantly reduce the circulating immunoglobulin complexes.[92] In developing countries where cost is the limiting factor, small volume PE may be used, but in India small volume PE was used by Tharakan *et al* with comparable results.[93] They used 15 mL/kg body weight/day to be continued till the progression of the disease got arrested or recovery started. This protocol is still performed in various centers in developing countries with good results.

Continuous flow PE is superior to intermittent flow exchanges. The replacement fluids do not affect the outcome of PE according to the French Study Group.[94] although albumin was found to be superior to fresh frozen plasma as the exchange fluid".

A better outcome was demonstrated with PE in French Study Group when compared with North American Study Group,[94] this is due to the fact that treatment was initiated within 2 weeks in the former study group and within 4 weeks in the latter therefore plasmapheresis is more beneficial when started within 7 days after disease onset rather than later, but was still beneficial in patients treated up to 30 days after disease onset.

All patients with mild, moderate, and severe GBS surely benefit. Plasmapheresis should be advised in patients who need even minimum assistance for walking, who are steadily progressing and those who are bed- and ventilator-bound . The role of plasmapheresis in children younger than 12 years is not yet known.

AAN in 2003 concluded that plasmapheresis hastens recovery in nonambulant patients who get treatment within 4 weeks of onset, and plasmapheresis hastens recovery of ambulant patients with GBS who are examined within 2 weeks plasmapheresis is usually administered as one plasma volume, 50 mL/kg, on 5 separate occasions over 1–2 weeks.[87].

But complications were slightly more observed in plasmapheresis group than the IVIg group. Significant adverse events of plasmapheresis include hypotension, septicemia, pneumonia, abnormal clotting, and hypocalcemia. Major hemostatic disorders, unstable cardiovascular state, active infection, and pregnancy are contraindications to PE.

Immunoadsorption therapy is an alternative technique to plasmapheresis. This form of therapy removes Ig from the circulation without the need for replacement with albumin or FFP because of loss of albumin. Evidence says that there is no difference in outcomes between patients treated with immunoadsorption and plasmapheresis or double filtration plasmapheresis .[95][96]

Role of Steroids

In a Cochrane systematic review of 6 trials with 587 patients it has been shown that corticosteroid therapy is ineffective for treating GBS .[97]

Intra venous immunoglobulin therapy

The first RCT on the use of IVIg was published in 1992, and showed that IVIg is as effective as PE.[98]. Since the publication of these results, IVIg, in a regimen of 0.4 g/kg bodyweight daily for 5 consecutive days, has replaced PE as the preferred treatment in many centers, mainly because of its greater convenience and availability. The Cochrane review on the use of IVIg in GBS contained 4 additional trials”.[97].No difference was found between IVIg and plasmapheresis with respect to the improvement in disability grade after 4 weeks, the duration of mechanical ventilation, mortality, or residual disability, the combination of plasmapheresis followed by IVIg was not significantly better than PE or IVIg alone and the combination of IVIg and intravenous methyl prednisolone was not more effective than IVIg alone, although there might be a short-term effect of this combined treatment when a correction is made for known prognostic factors.[98][99].

In general in patients with renal dysfunction the rate of infusion should be decreased to half of the normal infusion rate.

Timing of treatment

Most of the RCT have included only patients who are treated within the first 2 weeks from onset of weakness and who are unable to walk without assistance. If these criteria are met, there is no doubt that patients with GBS should be treated with IVIg or plasmapheresis. But in patients with rapidly progressive limb weakness or impaired pulmonary function but who are still able to walk, it seems better to treat these patients with IVIg but there is no definitive evidence.

A retrospective study on those patients who are able to walk with some support or no support showed that they often have residual disabilities.[98] , that no RCTs have assessed the effect of plasmapheresis or IVIg in these mildly affected patients with GBS.

Miller Fisher syndrome

No RCTs have studied the effect of plasmapheresis or IVIg in patients with MFS.[99] but observational studies have suggested that the final outcome in patients with MFS is generally good. In a large uncontrolled observational study,[100]IVIg slightly hastened the amelioration of ophthalmoplegia and ataxia and the investigators concluded that IVIg and PE did not influence the outcome of patients with MFS, presumably because of good natural recovery. Patients with mild or uncomplicated MFS may perhaps be treated conservatively. Patients with more severe or complicated anti-GQIB antibody syndrome, an overlapping GBS, should probably receive immunotherapy.

Some patients with GBS continue to deteriorate after plasmapheresis or a standard course of IVIg. In these cases, further option is unknown. Whether these patients need plasmapheresis after they have been treated with IVIg has not been investigated, but the combination of plasmapheresis followed by IVIg is no better than PE or IVIg alone, PE after IVIg is also not advised, because PE would probably wash out the IVIg previously administered. But a study in a small series of patients investigated the effect of a second course of IVIg in severe unresponsive patients with GBS.[101] this uncontrolled study suggested that a repeated course of IVIg could be effective. About 5%-10% of patients with GBS deteriorate after initial improvement or stabilization following IVIg treatment.[102]Although no RCTs have assessed the effect of a repeated IVIg dose in this condition, it is common practice to give a second IVIg course (2 g/kg in 2–5 days). These patients are thought to have a prolonged immune response that causes persistent nerve damage that needs treatment for a longer period of time.[103] A longer interval between onset of treatment and a longer time to nadir may be associated with a greater chance of relapse.

In places with restrictions in financial resources, especially in developing countries cost-effectiveness of any treatment becomes a major issue in treatment decision making. This is much applicable in GBS in which the currently approved treatment has shown equal efficacy. There are a few available cost analysis studies addressing this issue and the results are controversial.[104][105], However in developing countries use of small volume PE may bring down the cost when compared to IVIg hence the decision to use PE or IVIg must be based on multiple factors the main limitations for use of PE would be availability of the technical expertise and support. Lack of these, ease of administration, and fewer side effects with IVIg may dictate use of IVIg as the first line of therapy.

Prognosis and Outcome

GBS is acute life threatning illness with significant morbidity and mortality. Mortality rates vary between 1-18% and are higher in mechanically ventilated patients 12-20%. The major causes of mortality include pneumonia, sepsis, ARDS, autonomic instability. The important factors that predict mortality include age, dysautonomia, requirement of mechanical ventilation, severity of weakness at admission ,time to peak disability.[106]. GBS has a variable clinical course and outcome ,hence good disability assessment scale and prognostic parameters are required to predict the prognosis at the outset. The most commonly used scale is Hughes score (0-6) with 0-healthy,1-minor symptoms but capable of manual work, 2-able to walk without support but incapable of manual work, 3-able to walk with support, 4-bed/chair bound,5-require assisted ventilation and 6-dead.[107]

Factors such as increased age, presence of antecedent event especially diarrhea and high disability at nadir are frequently associated with poor outcomes. These parameters have been incorporated into EGOS-Erasmus GBS Outcome Scale which is used to predict outcome at 6 months. [108]Though majority of patients recover, 20% have severe disability and with a mortality rate of 5%.

Diagnostic criteria for acute demyelinating polyneuropathy

Features essential for establishing the diagnosis

- Progressive weakness of all four limbs which may vary from mild weakness to complete paralysis.
- Areflexia or diminished reflexes.

Features strongly supporting the diagnosis

- Progression of symptoms last for few days to four weeks.
- Relative symmetry of symptoms ranging from mild weakness to complete paralysis
- Mild sensory signs or symptoms.
- Involvement of cranial nerve , most common is facial nerve involvement especially bilateral symmetrical weakness of facial muscles and sometimes unilateral involvement. Occasionally 3, 4, 5, 6, 10, 11, 12 cranial nerves are involved.
- Recovery starts 2-4 wks after cessation of progression.
- Autonomic disturbunces can include increased heart rate, increased blood pressure, orthostatic hypotension, urinary disturbunces, cardiac arrhythmias.
- The antecedent events such as respiratory tract infections & GIT illness is common
- Features of increased concentration of proteins in the CSF with not more than 10 mononuclear cells per cubic mm.

Findings making the diagnosis doubtful

- Persistant asymmetry of signs and symptoms.
- Persistant bladder or bowel dysfunction.
- Presence of bladder or bowel dysfunction
- Presence of fever at onset of disease process.
- Definite sensory level.
- Involvement of lung with mild paresis
- Gradual progression of disease process with absence of respiratory involvement
- Chronic inflammatory demyelinating polyradiculapathy or sub acute polyradiculopathy

Features excluding the diagnosis

- Diagnosis like Botulism, Poliomyelitis, Mysthenia, or Toxic neuropathy (eg from dapsone, nitrofurantoin, or opc compound, lead)
- Recent diphtheria infection.
- HIV Disease.
- Diabetes mellitus.
- Acute Intermittent porphyria, due to abnormal porphyrin metabolism.

Electrophysiological classification of guillain-barre syndrome

(Hadden RD, Cornblath DR, Hughes, et al)

Neurophysiological criteria for acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor-sensory axonal neuropathy (AMSAN), acute motor axonal neuropathy (AMAN).

At least 3 sensory nerves and 3 motor nerves with multi-site stimulation F waves and bilateral tibial H reflexes need to be evaluated.

AIDP

- At least 1 of the following in each of at least 2 nerves, or at least 2 of the following in1 nerve if all others inexcitable and distal compound muscle action potential (dCMAP) >10% lower limit of normal (LLN).
- Motor conduction velocity <90% LLN (85% if dCMAP <50% LLN.
- Distal motor latency >110% upper limit of normal (ULN) (>120% if dCMAP <100%LLN).
- pCMAP/dCMAP ratio <0.5 and dCMAP>20%LLN.
- F-response latency >120% ULN.

AMSAN

- None of these features of AIDP except 1 demyelinating feature allowed in 1 nerve if dCMAP<10% LLN.
- Sensory action potential amplitudes less than LLN.

AMAN

- None of the features of AIDP except 1 demyelinating feature allowed in 1 nerve if dCMAP <10% LLN
- Sensory action potential amplitudes normal.

Electrodiagnostic (EDX) testing is done to support the clinical impression. EDX testing of patients with GBS often demonstrates features of demyelination, such as “temporal dispersion, significantly slow conduction velocities, and prolonged distal and F-wave latencies”.[115] Electrodiagnostic testing features of acquired demyelination like conduction block, temporal dispersion, nonuniform slowing of conduction velocities are particularly helpful because these findings are characteristic of immune-mediated demyelinating neuropathies. In early GBS, prolonged distal compound muscle action potential (CMAP) latencies and temporal dispersion are more commonly demonstrated than are slow motor conduction velocities and conduction block.[118] Another electrodiagnostic testing hallmark of GBS is the sural sparing pattern that is, the finding of a normal sural sensory nerve response in the setting of abnormal upper extremity sensory nerve results.[118]. This pattern is very unusual for neuropathies other than GBS. Sural sparing, a marker of demyelinating neuropathy, is more commonly seen in later, than in early stages of AIDP. Other electrodiagnostic testing abnormalities are frequently encountered in early GBS but they are less specific to GBS include absent H-reflexes, low motor nerve CMAP amplitudes on distal stimulation, and prolonged F-wave responses.[116][118]. It is reported that the H-reflex was absent in 97% of GBS patients within the first week of symptom onset. It should also be pointed out that motor electrodiagnostic testing findings are more often abnormal than sensory nerve results in early GBS. Blink reflex studies are often abnormal when there is facial nerve involvement.[117]. Phrenic nerve conduction studies can be used to predict respiratory failure and the need for ventilation.[119]. Reduced CMAP amplitudes of 0%–20% of the lower limit of normal carry a poor prognosis.[120]

The diagnostic yield of various neurophysiological criteria may vary in different subforms of Guillain–Barré syndrome, whose prevalence varies in different geographical areas. In a recent study the diagnostic sensitivity of Albers *et al*,[121] Cornblath,[122] Ho *et al*,[123] Dutch GBS Study Group,[124] Italian GBS Study Group,[125] and Albers and Kelly criteria[126] were evaluated and correlated with clinical subtypes of GBS, duration, severity, and outcome.[127] The sensitivity of nerve conduction study in the diagnosis of GBS and in different clinical subtypes of GBS was highest using Albers criteria (88.2%) and lowest using Cornblath criteria (39.2%). As per Ho *et al*, patients could be categorized into AIDP (86.3%), AMAN (7.8%), and AMSAN (5.9%).

MATERIALS & METHODS

MATERIALS AND METHODS

SOURCE OF STUDY

Data in the study consists of primary data collected by the principal investigator directly from the patients who are admitted in the Coimbatore Government Medical College and Hospital.

DESIGN OF STUDY: Prospective observational study.

PERIOD OF STUDY: One year, July 2016 - June 2017.

SAMPLE SIZE: 50

METHODOLOGY:

50 patients with GBS diagnosed clinically as per Asbury and Cornblath criteria were enrolled and followed up for one year. Various epidemiological, clinical and electrophysiological parameters were evaluated. Hughes motor scale was used to measure functional motor deficits. Factors associated with poor functional outcome and need for mechanical ventilation were determined.

Patients with adult age group were taken into study to predict the outcome Classification of patients as axonal or demyelinating subtype was based on electro diagnostic criteria of Hadden et al. CSF analysis of patients was done to analyse with elevated protein concentration with normal cell count. Diagnosis of GBS is mainly clinical. Hadden Hughes et al and Winner Hughes et al in their independent studies show that 80 % of the times there is albumino -

cytological dissociation inCSF of the patients with GBS . In our study out of 50 patients who underwent CSF examination, 45 had albumino-cytological dissociation. Anticedent infections of gastroenteritis should be diagnosed by history taking and clinical examination.

Medical research council (MRC) sum score was used for valuing the muscle strength from 0 to 5 in proximal, distal muscles, upper and lower limbs bilaterally score ranged from 60 (normal) to 0 (quadriplegic).

Cranial nerve involvement was examined clinically and noted along with respiratory muscle weakness, which was assessed for the need of mechanical ventilation,so that oxygen administration, non-invasive ventilation and SpO2 estimate of arterial oxygen saturation record. Single breath count test- Ask patient to count out loud after maximal inspiration. Ability to reach 50 indicates a normal respiratory function. Single breath count of less than 15 indicates a dangerous low forced vital capacity (FVC) Sensory system were examined by clinical examination and autonomic nervous system abnormalities like cardiovascular manifestations of GI motility , blood pressure and heart rate ,ECG were measured.

Complete blood count and peripheral smear was done in the study to rule out haematological malignancies. C-reactive protein and ESR was done to rule out the vasculitis neuropathy.

All the patients were uniformly treated with indigenous IVIg preparations available in the hospital during the course of treatment. Patients were evaluated throughout the course of disease from the time of admission, till time of discharge (maximum at one month). GBS disability score was used for evaluation of functional impact during discharge of patients and during follow up.

STATISTICAL ANALYSIS

All the dates were entered in a data collection sheet in an Excel format and analysed using IBM SPSS version 21.0 Software. Analysis of continuous data was performed using Unpaired t-test to compare mean number of days of IVIg and Chi square test for comparison of influence of various factors on final outcome. For analysis of categorical data, Kruskal Wallis Test for analysis of functional outcome. Numerical values were reported using mean and standard deviation or median. Categorical values are reported using number and percentages. Probability value (p) value less than 0.05 was considered a statistically significant.

Hughes grade scale for assessing functional motor deficits

0	A healthy state
1	Minor symptoms or signs of neuropathy but capable of manual work/capable of running
2	Able to walk without support of a stick (5m across an open space) but incapable of manual work/running
3	Able to walk with a stick, appliance or support (5m across an open space)
4	Confined to bed or chair bound

5	Requiring assisted ventilation (for any part of the day or night)
6	Death

Medical Research Council (MRC)sum score[171]

The total MRC sum score ranges from 0 (total paralysis) to 60 (normal strength). The score is the sum of the MRC score of 6 muscles (3 at the upper and 3 at the lower limbs) on both sides, each muscle graded from 0 to 5. The following muscles were examined:

- Deltoid
- Biceps
- Wrist extensor
- Ileopsoas
- Quadriceps femoris
- Tibialis anterior

MRC-Muscle Grading Scale

Grade	Degree of Strength
5	Normal Strength
4	Ability to resist against moderate pressure throughout range of motion
3	Ability to move through full range of motion against gravity. If a subject has a contracture that limits joint movement, the mechanical range will be to the point at which the contracture causes joint restriction
2	Ability to move through full range of motion with gravity eliminated
1	A flicker of motion is seen or felt in the muscle
0	No movement

INCLUSION CRITERIA

1) Patients (Both Genders) of 50 numbers diagnosed on clinical examination of Asbury & Cornblath criteria at Coimbatore Medical College Hospital .
2) To use electro physiological tests & CSF analysis in aiding diagnosis

EXCLUSION CRITERIA

1) Patients with Toxic neuropathy
2) Vasculitis Neuropathy
3) Hametological Malignancies
4) HIV
5) Infectious Polyradiculopathy.

In our study results we have graded patients from 1 to 4 based on the MRC sum scoring scale of power in ranges.

GRADE	**MRC SSS**
1	0-19
2	20-29
3	30-39
4	$\geq$ 40

Followed by Patients with MRC sum score power range improvement along with grade improvement.

GRADE IMPROVEMENT	**MRC SSS IMPROVEMENT**
1 TO 2	10 TO 29
1 TO 3	1O TO 39
1 TO 4	10 TO 60
2 TO 3	20 TO 39
2 TO 4	20 TO 60

RESULTS

RESULTS

Table 1 : AGE DISTRIBUTION

AGE(IN YRS)	NO OF PATIENT	PERCENTAGE
< 30	18	36%
31-45	13	13%
46-60	12	24%
> 60	7	14%

Figure 1 : AGE DISTRIBUTION

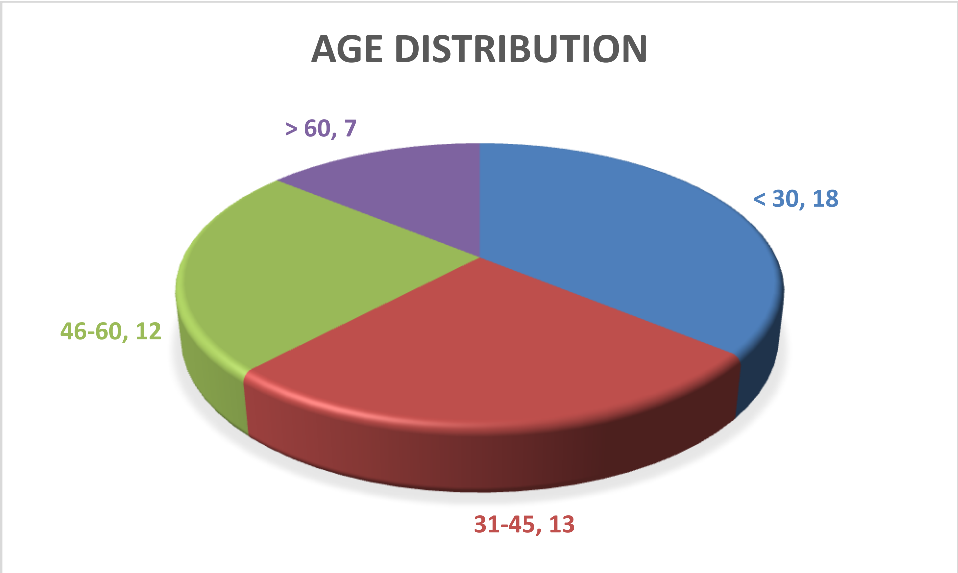


Table 2 : SEX DISTRIBUTION

SEX	NO OF PATIENT	PERCENTAGE
MALE	29	58%
FEMALE	21	42%

Figure 2.SEX DISTRIBUTION

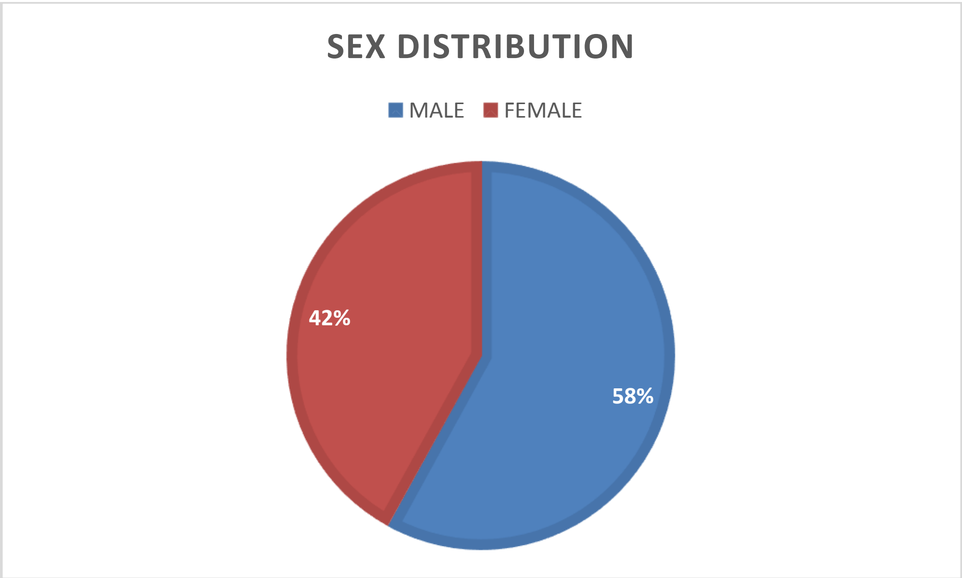


Table 3 :TIME INTERVAL FROM ONSET TO ADMISSION

TIME INTERVAL	NO OF PATIENTS	PERCENTAGE
< 24 HRS	35	70%
> 24HRS	15	30%

Figure 3 : TIME INTERVAL FROM ONSET TO ADMISSION

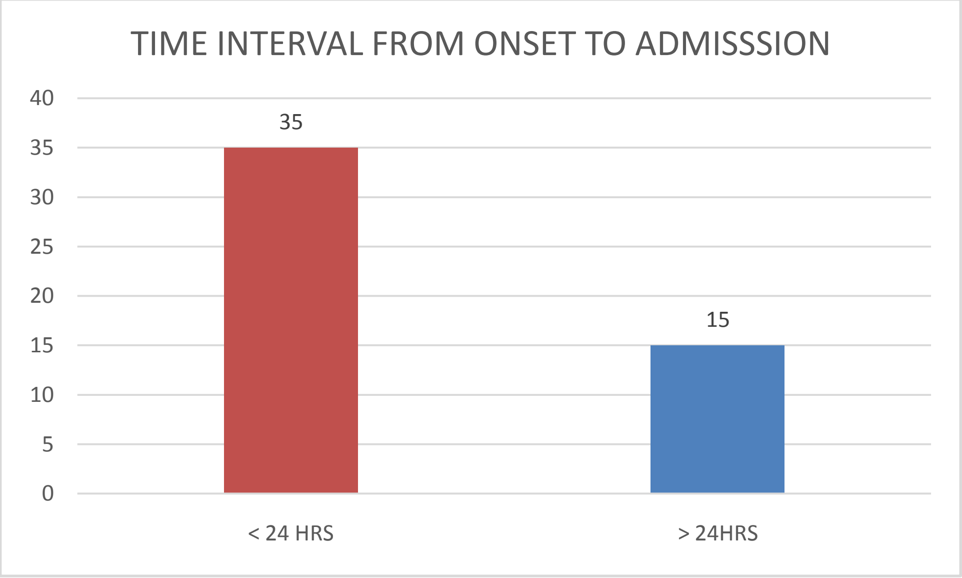


Table 4 : POWER AT ADMISSION

POWER AT ADMISSION	NO OF PATIENTS	PERCENTAGE
ONE	24	48%
TWO	26	52%
THREE	0	0%
FOUR	0	0%

Figure 4 : POWER AT ADMISSION

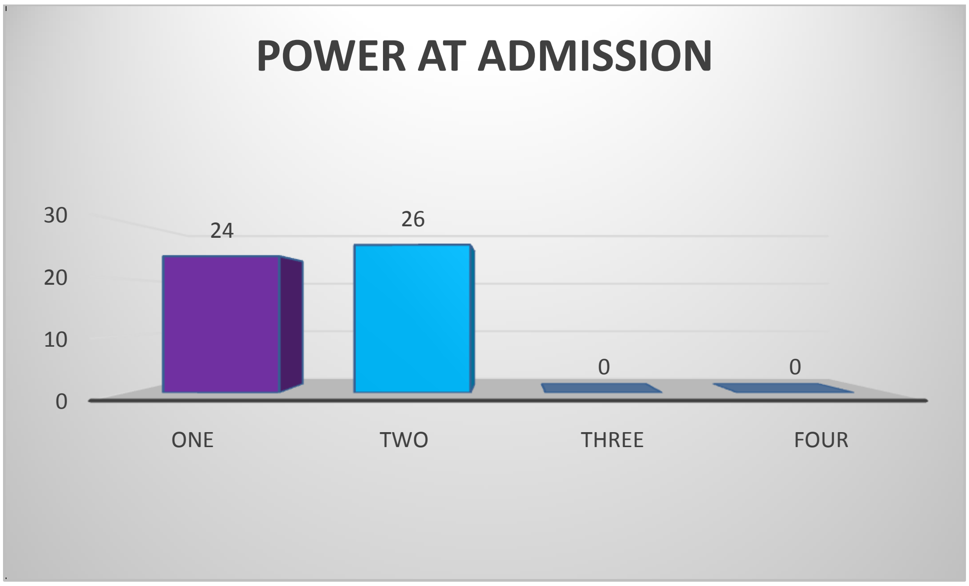


Table 5 : POWER AT DISCHARGE

POWER AT DISCHARGE	NO OF PATIENTS	PERCENTAGE
ONE	0	0%
TWO	0	0%
THREE	17	37%
FOUR	29	63%

Figure 5 :POWER AT DISCHARGE

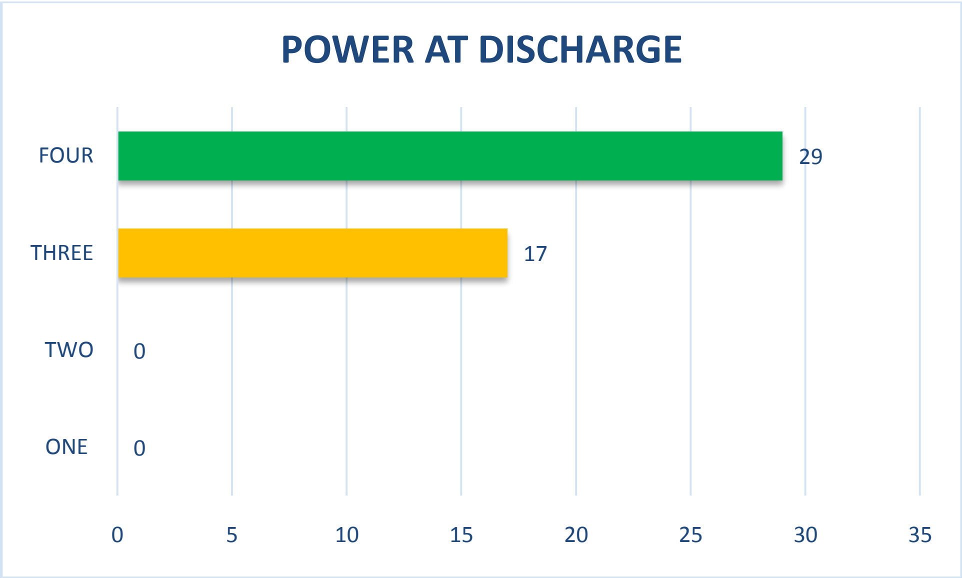


Table 6 : POWER AT ADMISSION AND DISCHARGE

POWER	ADMISSION	DISCHARGE
ONE	24	0
TWO	26	0
THREE	0	17
FOUR	0	29

Figure 6 :POWER BEFORE AND AFTER IVIg

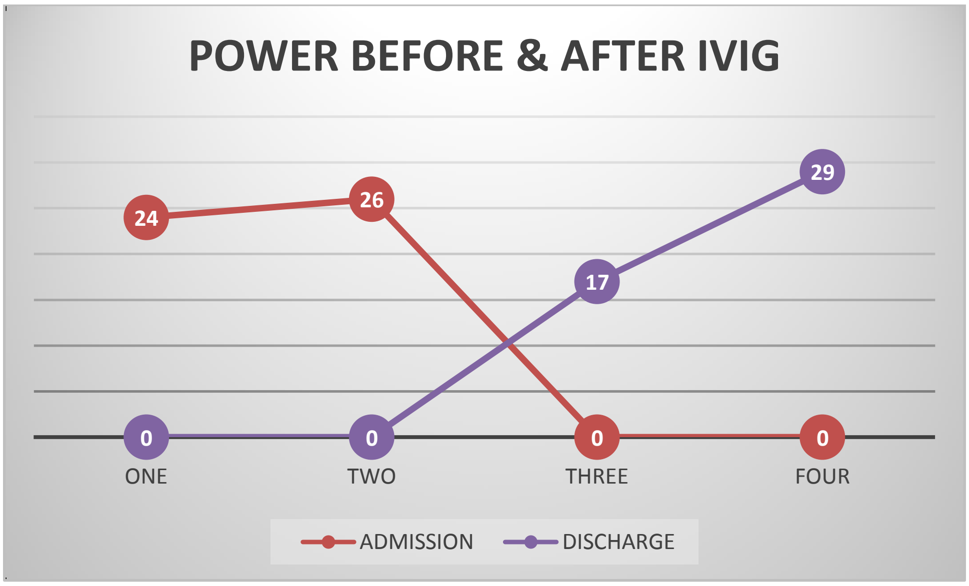


Table 7 : RESPIRATORY DIFFICULTY PRESENTATION

RESPIRATORY DIFFICULTY	NO OF PATIENTS	PERCENTAGE
PRESENT	15	30%
ABSENT	35	70%

Figure 7 : RESPIRATORY DIFFICULTY PRESENTATION

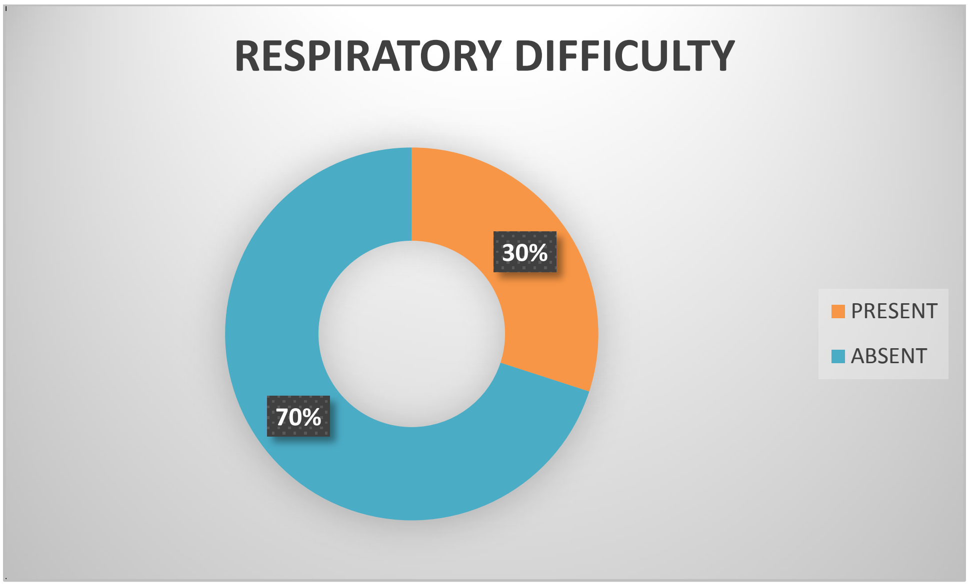


Table 8 : NEED OF VENTILLATORY SUPPORT

VENTILATORY SUPPORT	NO OF PATIENTS	PERCENTAGE
PRESENT	9	18%
ABSENT	41	82%

Figure 8 : NEED OF VENTILLATORY SUPPORT

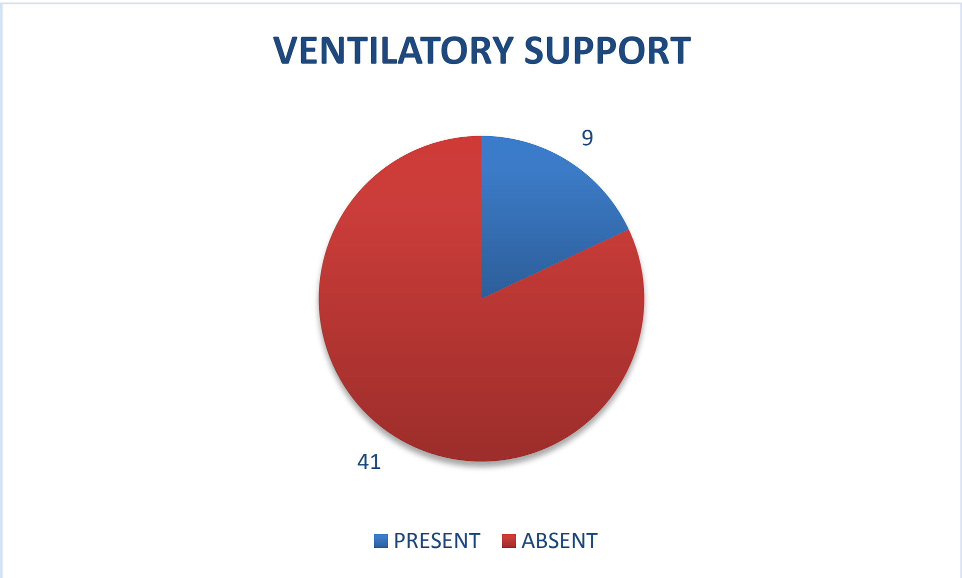


Table 9 : NUMBER OF DAYS OF IVIg GIVEN

IVIG - NO OF DAYS	NO OF PATIENTS	PERCENTAGE
THREE	9	18%
FIVE	38	76%
SEVEN	3	6%

Figure 9 :NUMBER OF DAYS OF IVIg GIVEN

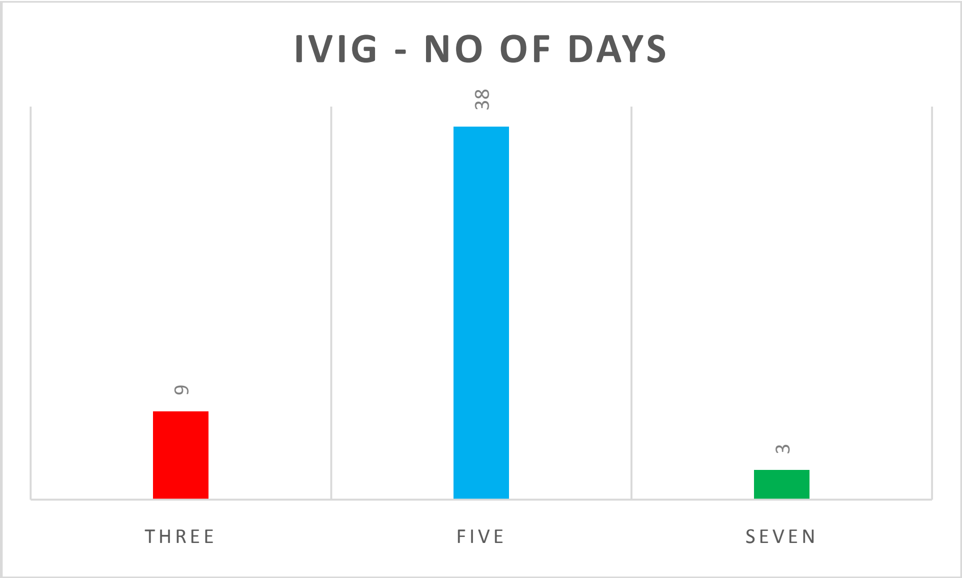


Table 10 :TYPE OF NEUROPATHY

TYPE OF NEUROPATHY	NO OF PATIENTS	PERCENTAGE
AIDP	45	90%
AMAN	5	10%

Figure 10 : TYPE OF NEUROPATHY

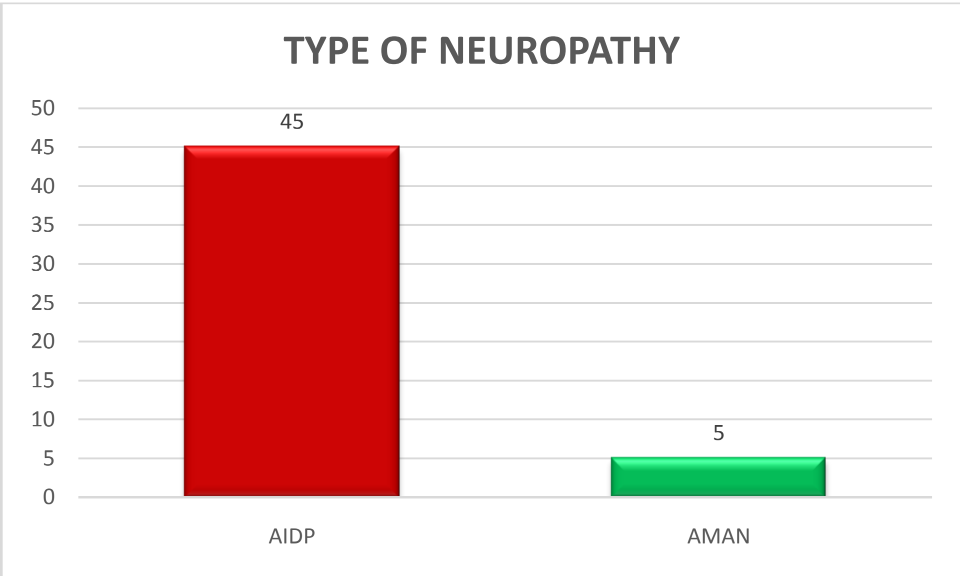


Table 11 : CRANIAL NERVE INVOLVEMENT

CRANIAL NERVE INVOLVED	NO PATIENTS	PERCENTAGE
PRESENT	15	30%
ABSENT	35	70%

Figure 11 ; CRANIAL NERVE INVOLVEMENT

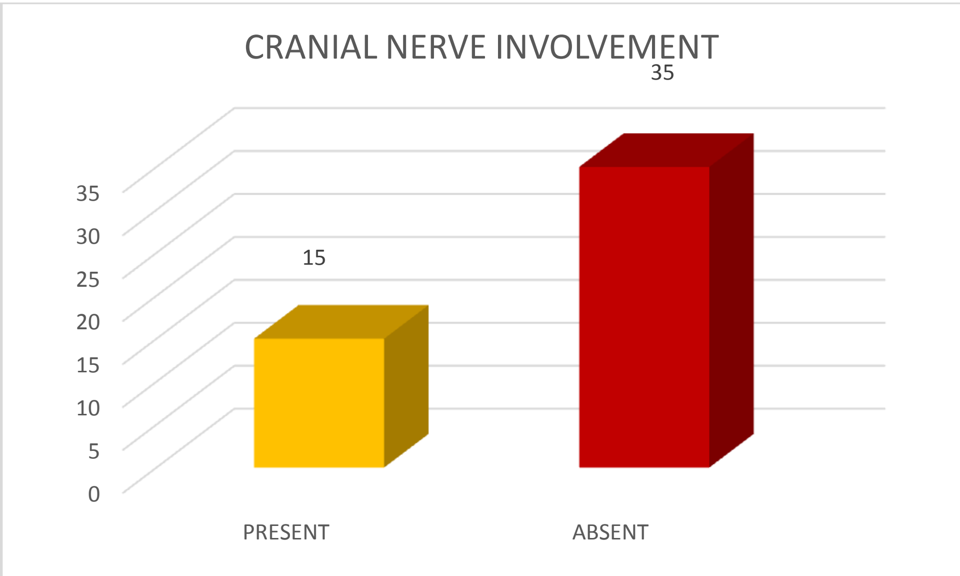


Table 12 : AUTONOMIC NERVOUS SYSTEM INVOLVEMENT

AUTONOMIC INVOLVEMENT	NO OF PATIENTS	PERCENTAGE
PRESENT	9	18%
ABSENT	41	82%

Figure 12 : AUTONOMIC NERVOUS SYSTEM INVOLVEMENT

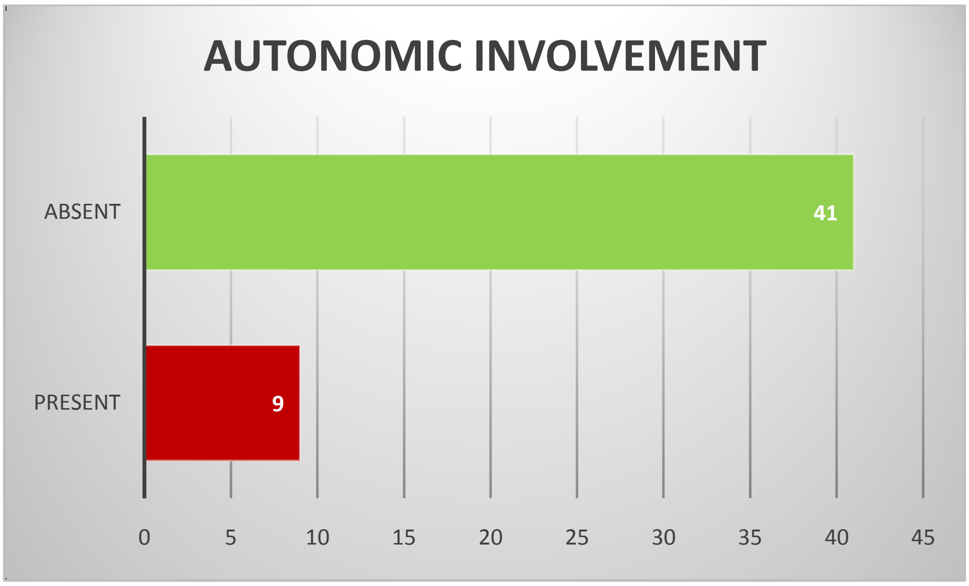


Table 13 : FINAL END POINT

END POINT	NO OF PATIENTS	PERCENTAGE
DEAD	4	8%
ALIVE	46	92%

Figure 13 : FINAL END POINT

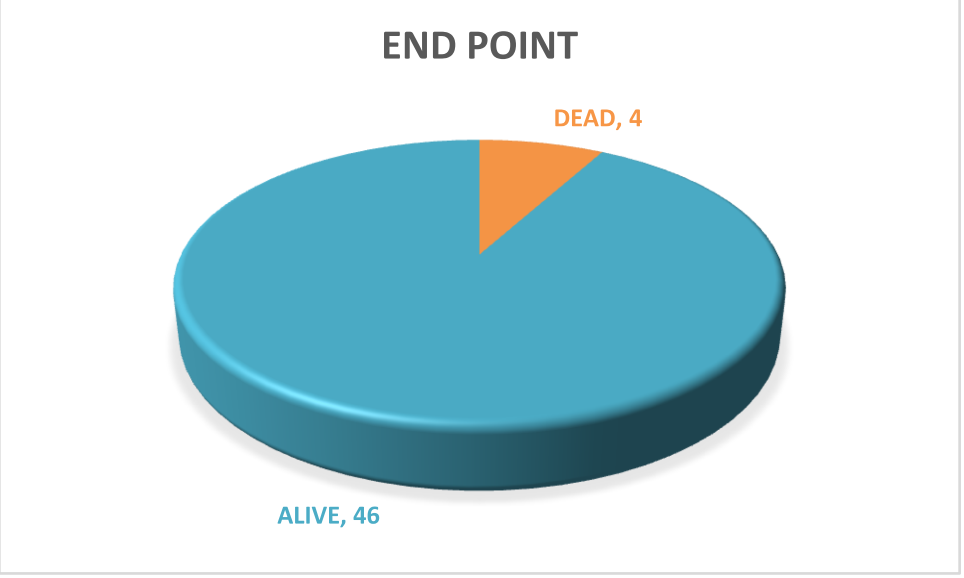
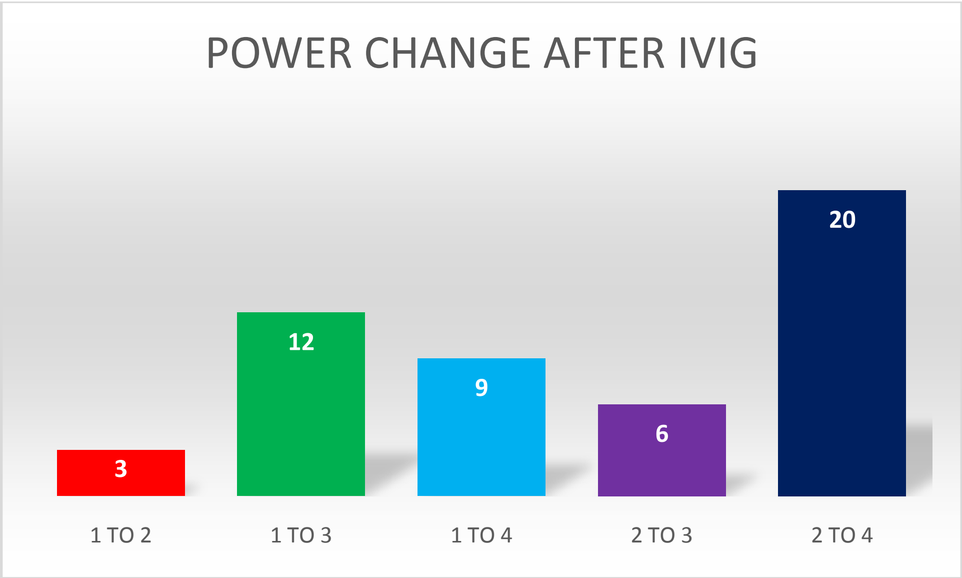


Table 14 : POWER CHANGE AFTER IVIg

POWER CHANGE AFTER IVIg	NO OF PATIENTS	PERCENTAGE
1 TO 2	3	6%
1 TO 3	12	24%
1 TO 4	9	18%
2 TO 3	6	12%
2 TO 4	20	40%

Figure 14 : POWER CHANGE AFTER IVIg.

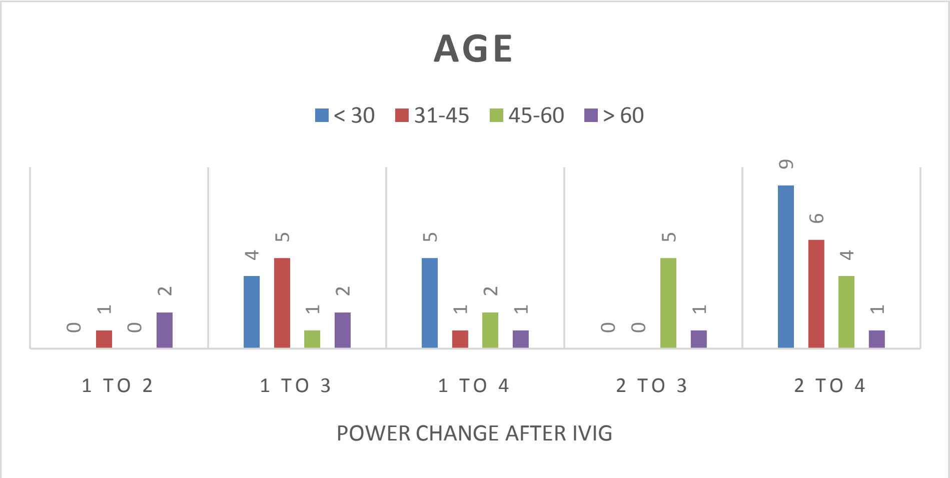


INFLUENCE OF VARIOUS FACTORS ON IMPROVEMENT IN POWER

Table 15 : INFLUENCE OF AGE ON IMPROVEMENT IN POWER

	AGE			
POWER CHANGE AFTER IVIg	**< 30**	**31-45**	**45-60**	**> 60**
1 TO 2	0	1	0	2
1 TO 3	4	5	1	2
1 TO 4	5	1	2	1
2 TO 3	0	0	5	1
2 TO 4	9	6	4	1
P VALUE - 0.009				
SIGNIFICANT				
KRUSKAL WALLIS TEST				

Figure 15 : INFLUENCE OF AGE ON IMPROVEMENT IN POWER



There is significant influence of age with patient's age less than 30 have better improvement in power which is also statistically significant with p value of 0.009.

Table 16 : IMPROVEMENT OF POWER CHANGE AFTER IVIg

	SEX	
POWER CHANGE AFTER IVIg	**MALE**	**FEMALE**
1 TO 2	3	0
1 TO 3	7	5
1 TO 4	7	2
2 TO 3	5	1
2 TO 4	7	13
P VALUE - 0.049		
SIGNIFICANT		
KRUSKAL WALLIS TEST		

There is significant influence of sex on improvement of power which is also statistically significant with p value of 0.049

Figure 16 : IMPROVEMENT OF POWER CHANGE AFTER IVIg

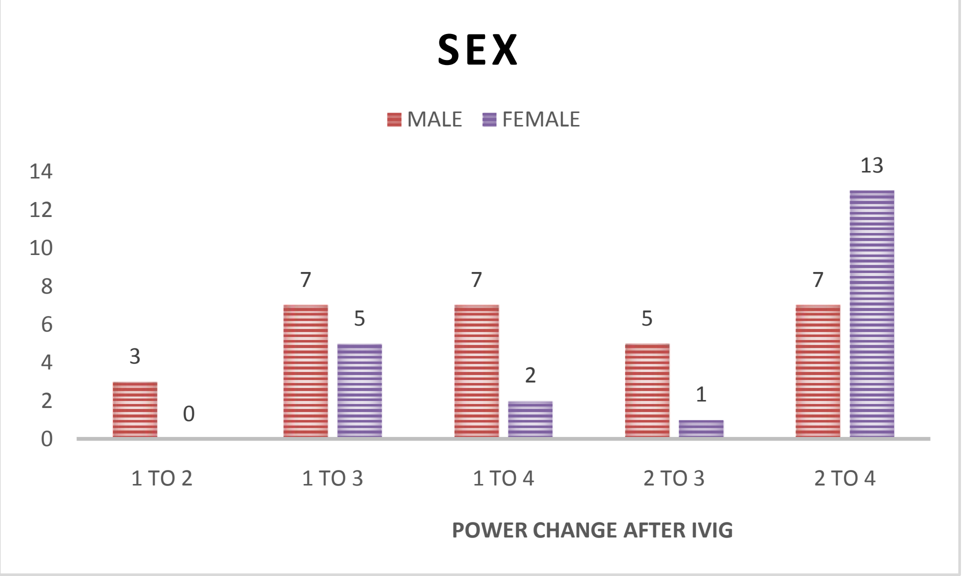


Table 17 : TIME OF ONSET TO ADMISSION AND IMPROVEMENT OF POWER

	TIME OF ONSET TO ADMISSION	
POWER CHANGE AFTER IVIg	**< 24 HRS**	**> 24 HRS**
1 TO 2	2	1
1 TO 3	7	5
1 TO 4	8	1
2 TO 3	5	1
2 TO 4	13	7
P VALUE - 0.046		
SIGNIFICANT		
KRUSKAL WALLIS TEST		

There is significant influence of time interval between on set to admission with patients admitted before 24 hrs have better improvement in power which is also statistically significant with P value of 0.046.

Figure 17 : TIME OF ONSET TO ADMISSION AND IMPROVEMENT OF POWER

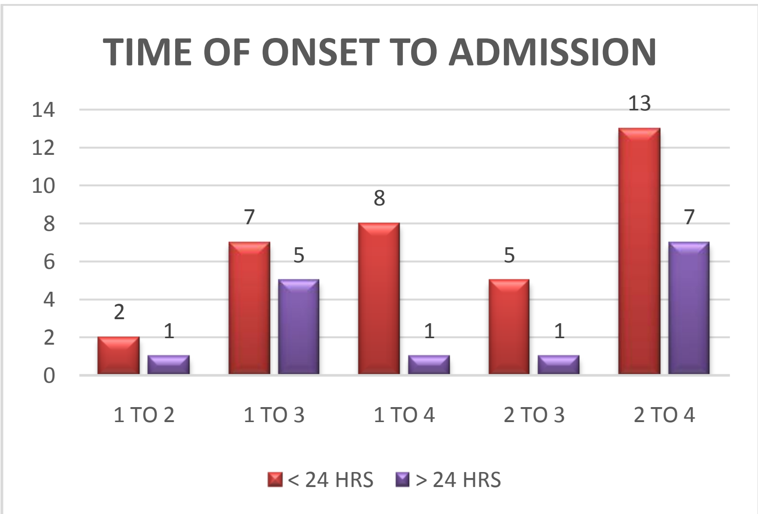


Table 18 : PATIENTS WITH RESPIRATORY DIFFICULTY AND IMPROVEMENT OF POWER

	RESPIRATORY DIFFICULTY	
POWER CHANGE AFTER IVIg	**PRESENT**	**ABSENT**
1 TO 2	3	0
1 TO 3	3	9
1 TO 4	1	8
2 TO 3	3	3
2 TO 4	5	15
P VALUE - 0.040		
SIGNIFICANT		
KRUSKAL WALLIS TEST		

There is significant influence of respiratory distress with there is better improvement in patient who doesn't has respiratory distress which is also statistically significant with p value of 0.040

Figure 18 : PATIENTS WITH RESPIRATORY DIFFICULTY AND IMPROVEMENT OF POWER

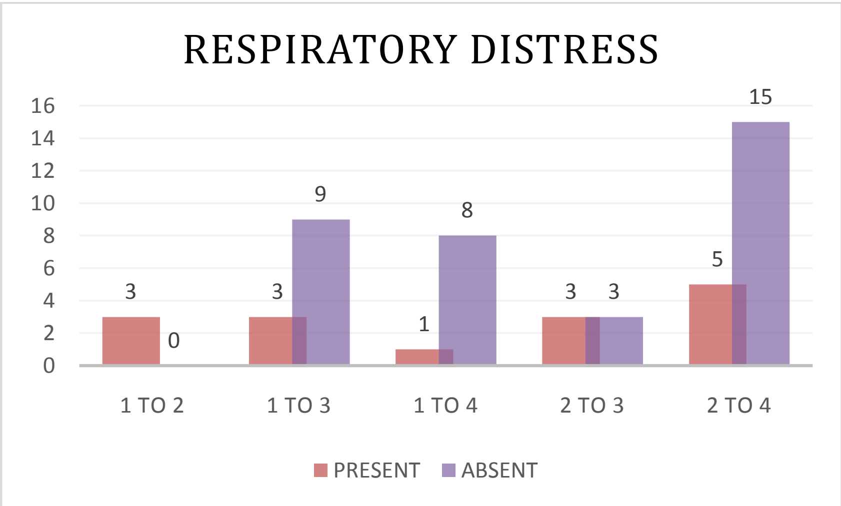


Table 19 : PATIENTS WITH VENTILLATORY SUPPORT IMPROVEMENT OF POWER

	VENTILATORY SUPPORT	
POWER CHANGE AFTER IVIg	**PRESENT**	**ABSENT**
1 TO 2	3	0
1 TO 3	1	4
1 TO 4	1	8
2 TO 3	2	4
2 TO 4	2	18
P VALUE -0.002		
SIGNIFICANT		
KRUSKAL WALLIS TEST		

There is significant influence of ventilator support with there is better improvement in patient who doesn't end up in requiring ventilator support which is also statistically significant with p value of 0.002.

Figure 19 : PATIENTS WITH VENTILLATORY SUPPORT IMPROVEMENT OF POWER

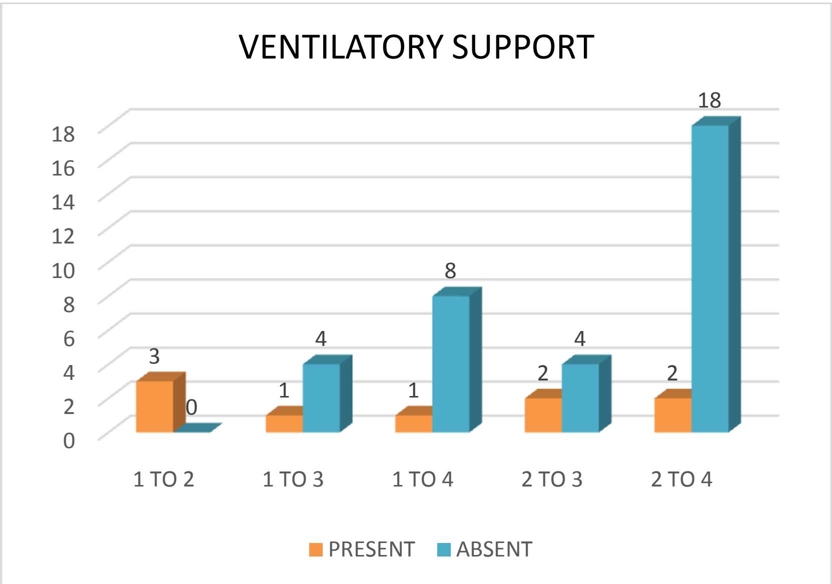


Table 20 : NUMBER OF DAYS IVIg AND IMPROVEMENT OF POWER

	NO OF DAYS OF IVIg		
POWER CHANGE AFTER IVIg	**THREE**	**FIVE**	**SEVEN**
1 TO 2	0	3	0
1 TO 3	3	8	1
1 TO 4	2	7	0
2 TO 3	1	3	2
2 TO 4	3	17	0
P VALUE - 0.166			
NON SIGNIFICANT			
KRUSKAL WALLIS TEST			

There is no significant influence of no of days of IVIg over improvement of power.

Figure 20 : NUMBER OF DAYS IVIg AND IMPROVEMENT OF POWER

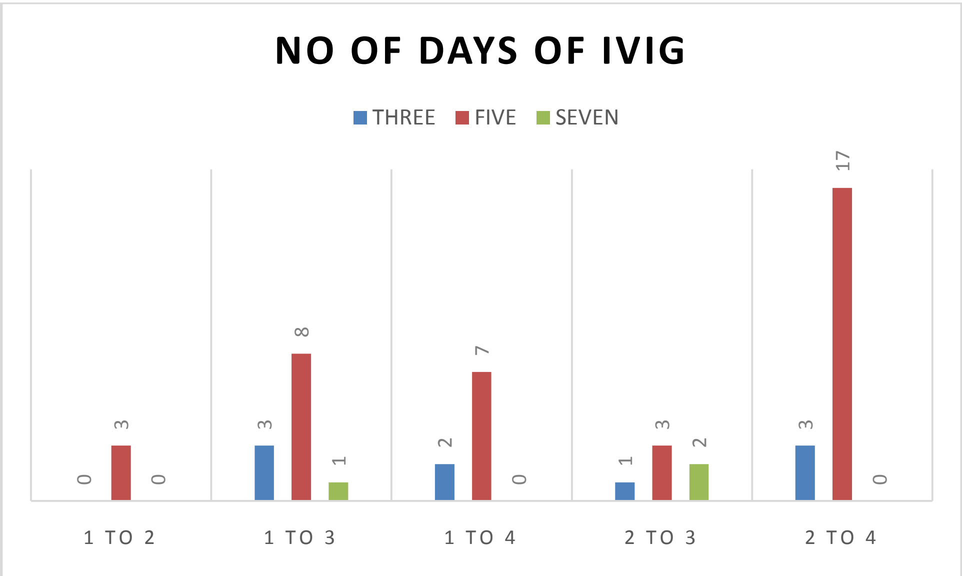


Table 21 : MEAN NUMBER OF DAYS OF IVIg AND IMPROVEMENT OF POWER

	MEAN NO OF DAYS OF IVIg	
POWER CHANGE AFTER IVIg	**MEAN**	**SD**
1 TO 2	5	0
1 TO 3	4.67	1.15
1 TO 4	4.56	0.88
2 TO 3	5.33	1.5
2 TO 4	4.7	0.73
P VALUE - 0.586		
NON SIGNIFICANT		
ANOVA		

There is no significant influence mean no of days of requirement of IVIg over functional outcome (improvement in power).

Figure 21 : MEAN NUMBER OF DAYS OF IVIg AND IMPROVEMENT OF POWER

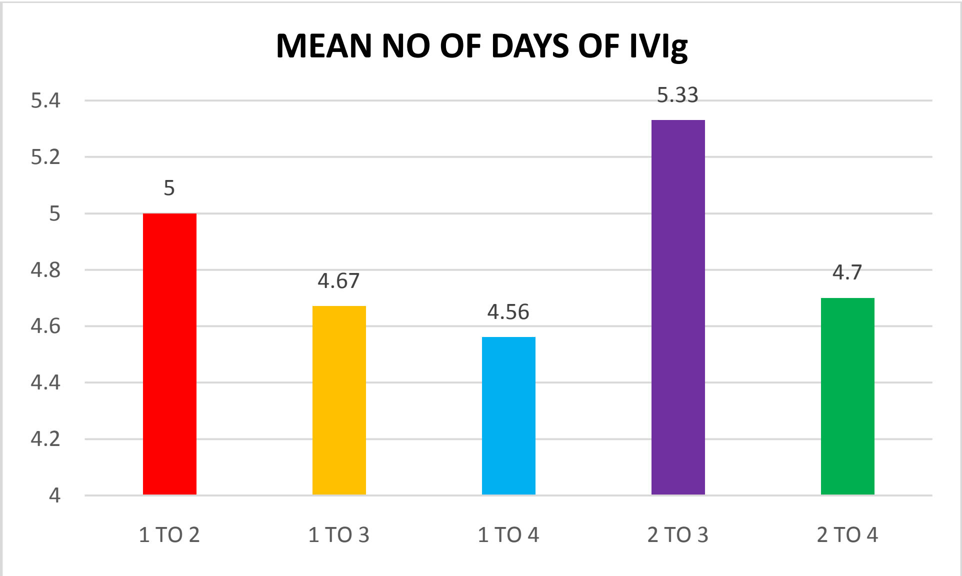


Table 22 : TYPE OF NEUROPATHY AND IMPROVEMENT OF POWER

	TYPE OF NEUROPATHY	
POWER CHANGE AFTER IVIg	**AMAN**	**AIDP**
1 TO 2	2	1
1 TO 3	1	11
1 TO 4	0	9
2 TO 3	2	4
2 TO 4	0	20
P VALUE -0.001		
SIGNIFICANT		
KRUSKAL WALLIS TEST		

There is significant influence of type of neuropathy with patient's with AIDP have better improvement which is also statistically significant with p value of 0.001

Figure 22 : TYPE OF NEUROPATHY AND IMPROVEMENT OF POWER.

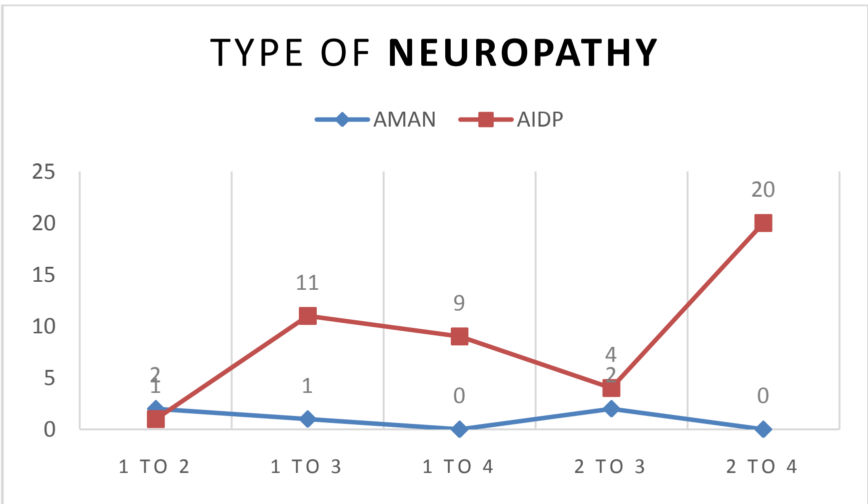


Table 23 : CRANIAL NERVE IMPROVEMENT AND IMPROVEMENT OF POWER

	CRANIAL NERVE INVOLVEMENT	
POWER CHANGE AFTER IVIg	**PRESENT**	**ABSENT**
1 TO 2	2	1
1 TO 3	4	8
1 TO 4	0	9
2 TO 3	2	4
2 TO 4	7	13
P VALUE - 0.191		
NON SIGNIFICANT		
KRUSKAL WALLIS TEST		

There is no significant influence of cranial nerve involvement on functional outcome

Figure 23 : CRANIAL NERVE IMPROVEMENT AND IMPROVEMENT OF POWER

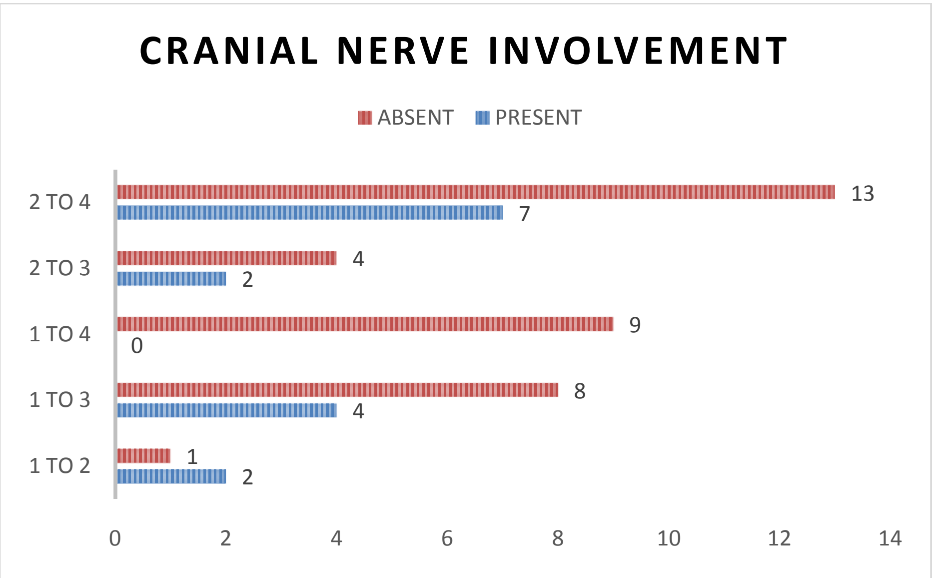


Table 24 : AUTONOMIC INVOLVEMENT AND IMPROVEMENT OF POWER

	AUTONOMIC INVOLVEMENT	
POWER CHANGE AFTER IVIg	**PRESENT**	**ABSENT**
1 TO 2	3	0
1 TO 3	1	4
1 TO 4	2	7
2 TO 3	1	5
2 TO 4	2	18
P VALUE - 0.004		
SIGNIFICANT		
KRUSKAL WALLIS TEST		

There is significant better improvement of power with autonomic system involvement which is also statistically significant with p value of 0.004.

Figure 24 : AUTONOMIC INVOLVEMENT AND IMPROVEMENT OF POWER

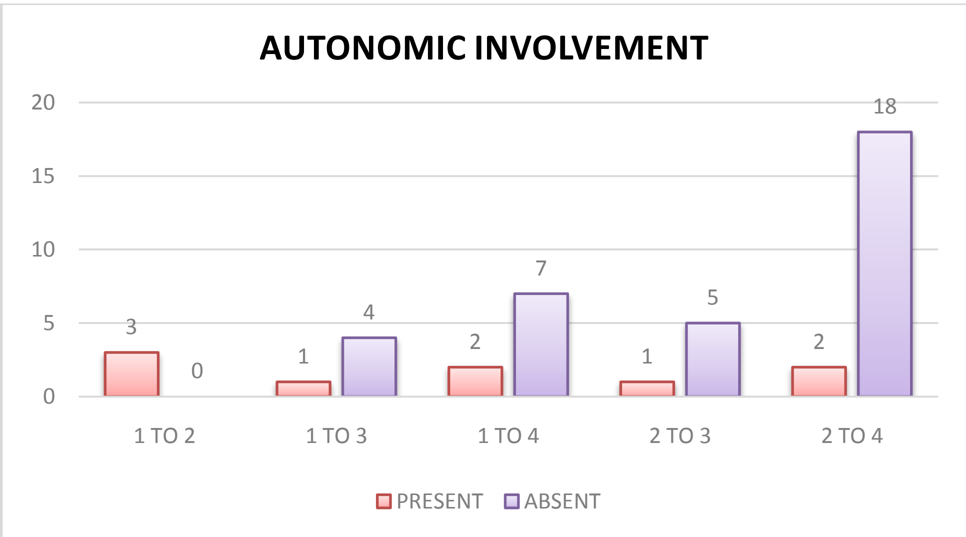


Table 25 : AGE FACTOR AND END POINT

	END POINT	
AGE	**DEATH**	**ALIVE**
<30	0	18
31-45	1	12
46-60	1	11
>60	2	15
P VALUE - 0.133		
NON SIGNIFICANT		
KRUSKAL WALLIS TEST		

There is no significant influence of age over final endpoint (Death) with p value of 0.133.

Figure 25 : AGE FACTOR AND END POINT.

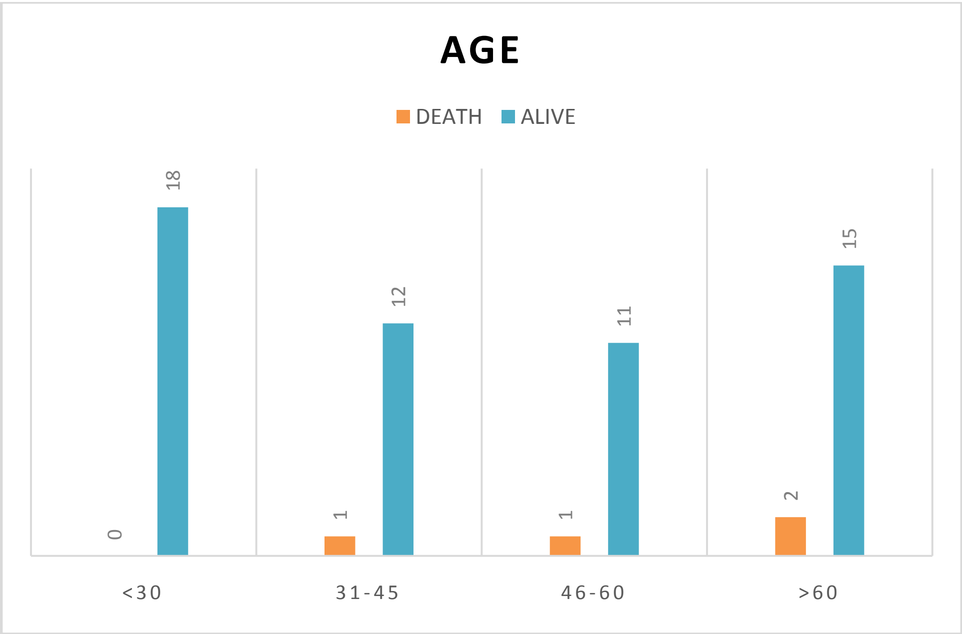


Table 26 : SEX DISTRIBUTION AND END POINT

	END POINT	
SEX	**DEATH**	**ALIVE**
MALE	4	25
FEMALE	0	21
P VALUE - 0.076		
NON SIGNIFICANT		
CHI SQUARE TEST		

There is no significant influence of sex over final endpoint (Death) with p value of 0.076.

Figure 26 : SEX DISTRIBUTION AND END POINT

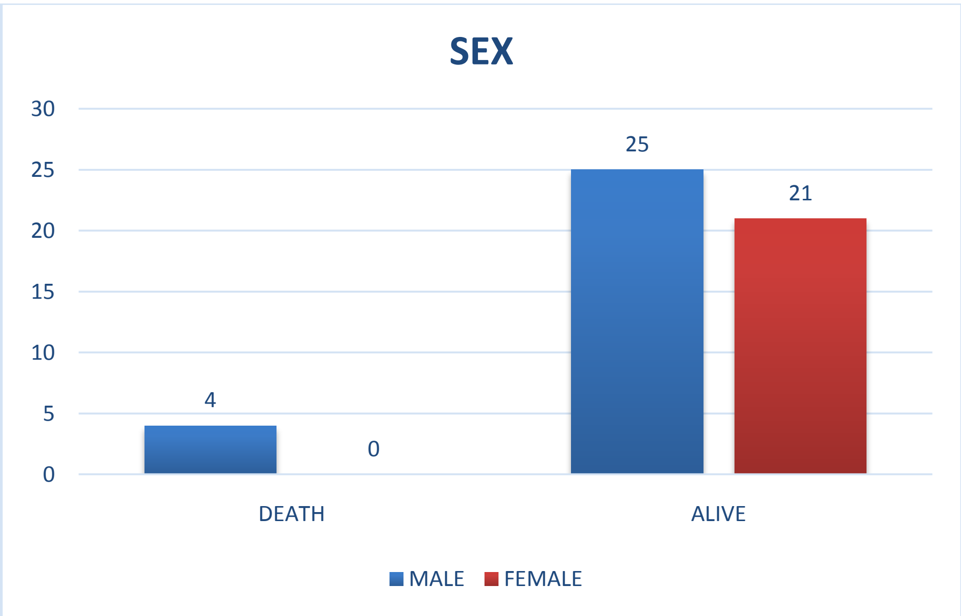


Table 27 : TIME OF ONSET TO ADMISSION AND END POINT

	END POINT	
TIME OF ONSET TO ADMISSION	**DEATH**	**ALIVE**
< 24 HRS	3	32
> 24 HRS	1	14
P VALUE - 0.820		
NON SIGNIFICANT		
CHI SQUARE TEST		

There is no significant influence of time of onset to admission over final endpoint (Death) with p value of 0.820.

Figure 27 : TIME OF ONSET TO ADMISSION AND END POINT

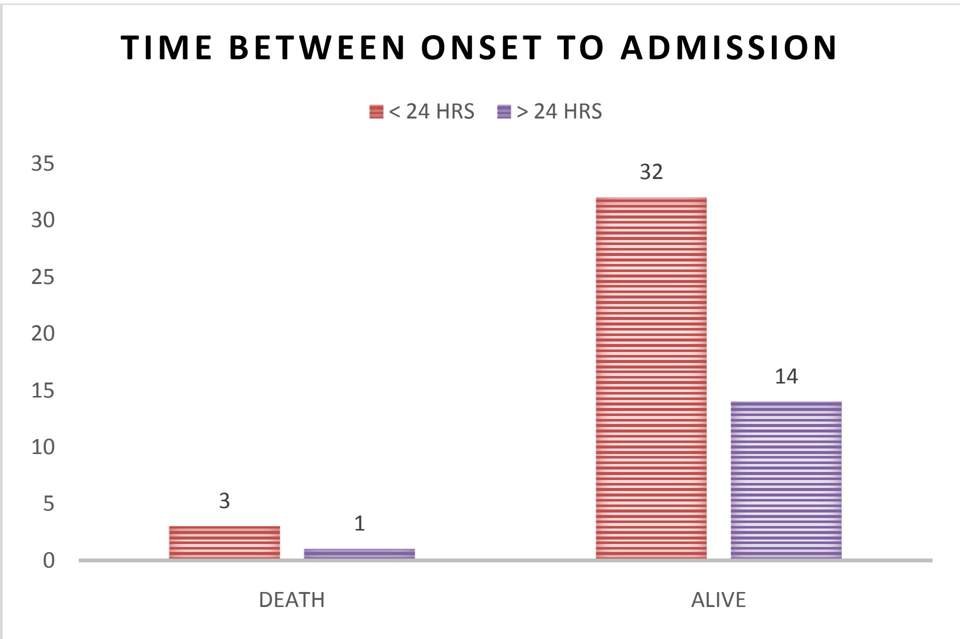


Table 28 : RESPIRATORY DIFFICULTY AND END POINT

	END POINT	
RESPIRATORY DIFFICULTY	**DEATH**	**ALIVE**
PRESENT	4	11
ABSENT	0	35
P VALUE - 0.001		
SIGNIFICANT		
CHI SQUARE TEST		

There is significant influence of respiratory difficulty over final endpoint (Death) with p value of 0.001 which is statistically significant. Patients who end up in mortality have more chance of respiratory difficulty.

Figure 28 : RESPIRATORY DIFFICULTY AND END POINT

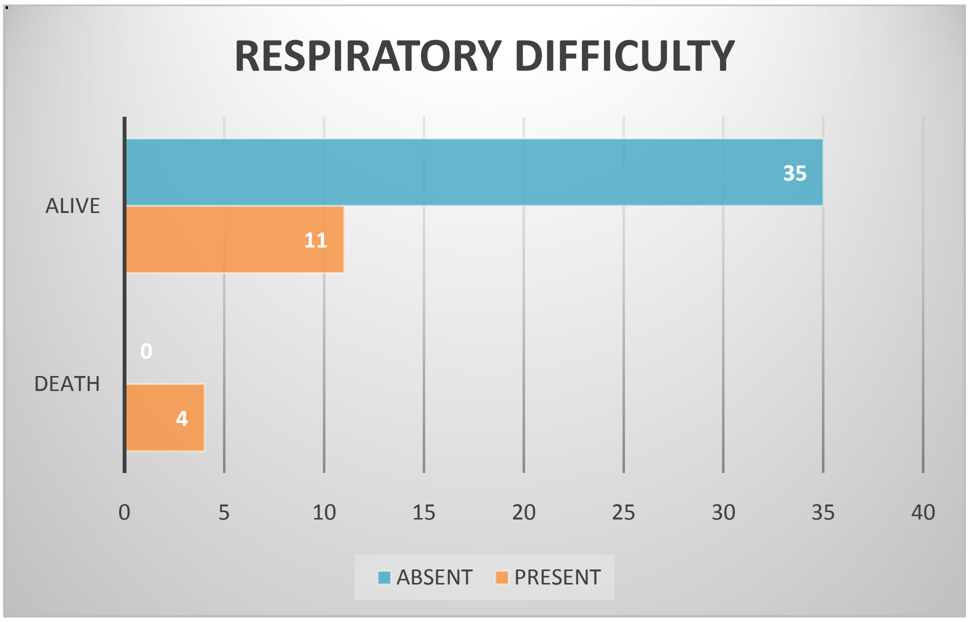


Table 29 : VENTILATORY SUPPORT AND END POINT

	END POINT	
VENTILATORY SUPPORT	**DEATH**	**ALIVE**
YES	4	5
NO	0	41
P VALUE - 0.001		
SIGNIFICANT		
CHI SQUARE TEST		

There is significant relation between requirements of ventilator support over final endpoint (Death) with p value of 0.001.Patient having more chance of mortality require ventilator support.

Figure 29 : VENTILATORY SUPPORT AND END POINT

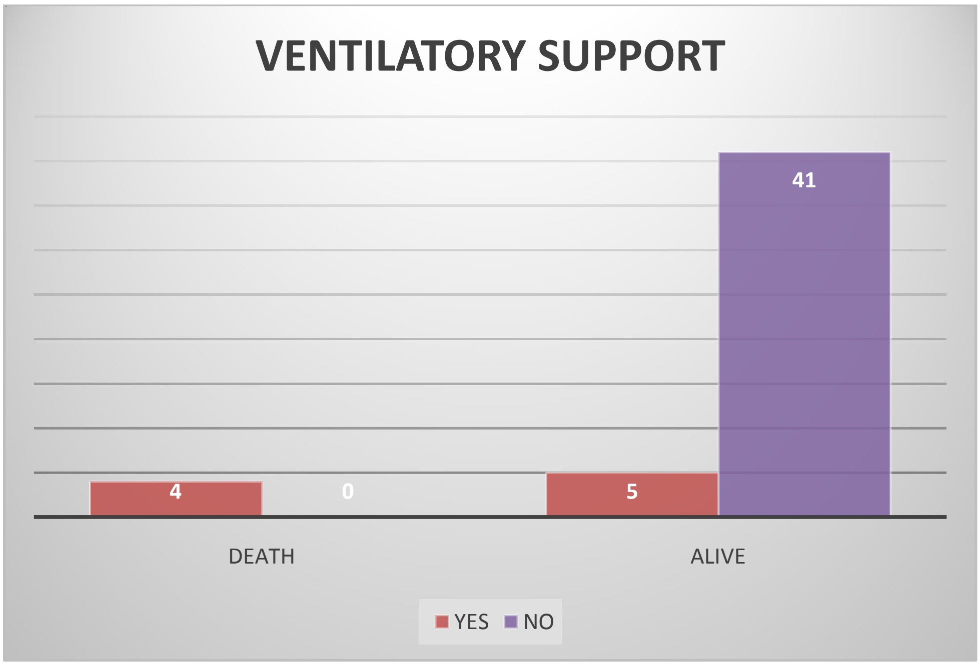


Table 30 : MEAN AND SD FOR NUMBER OF DAYS OF IVIg AND END POINT

	END POINT	
NO OF DAYS OF IVIg	**DEATH**	**ALIVE**
MEAN	5.5	4
SD	0.9	1.2
P VALUE - 0.109		
NON SIGNIFICANT		
UNPAIRED T TEST		

There is no significant influence of mean no of days of IVIg over final endpoint (Death) with p value of 0.109.

Figure 30 : MEAN NUMBER OF DAYS OF IVIg AND END POINT

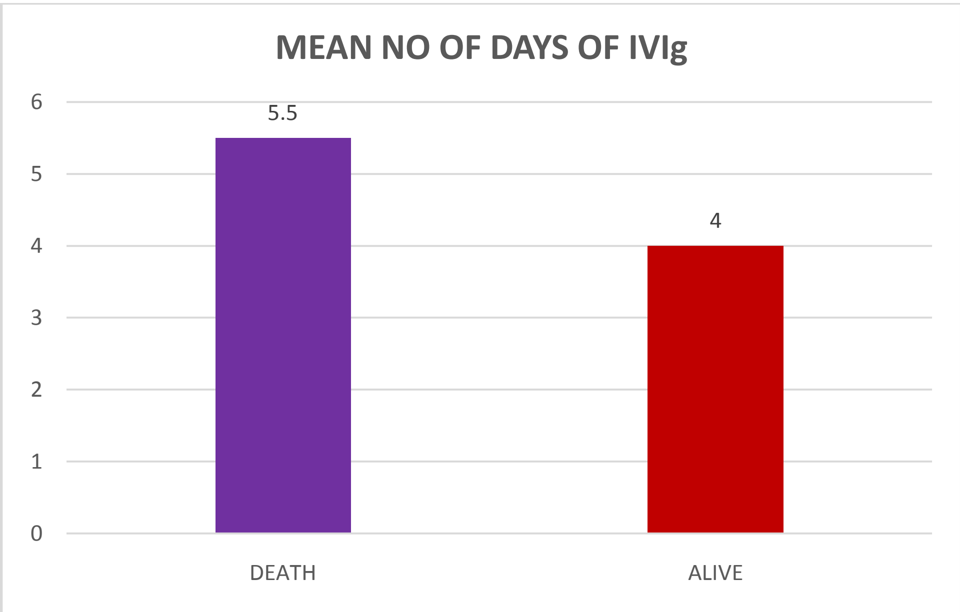


Table 31 : NUMBER OF DAYS POF IVIg AND END POINT

	END POINT	
NO OF DAYS OF IVIG	**DEATH**	**ALIVE**
THREE	0	9
FIVE	3	35
SEVEN	1	2
P VALUE - 0.183		
NON SIGNIFICANT		
KRUSKAL WALLIS TEST		

There is no significant influence of no of days of IVIg over final endpoint (Death) with p value of 0.133.

Figure 31 : NUMBER OF DAYS POF IVIg AND END POINT

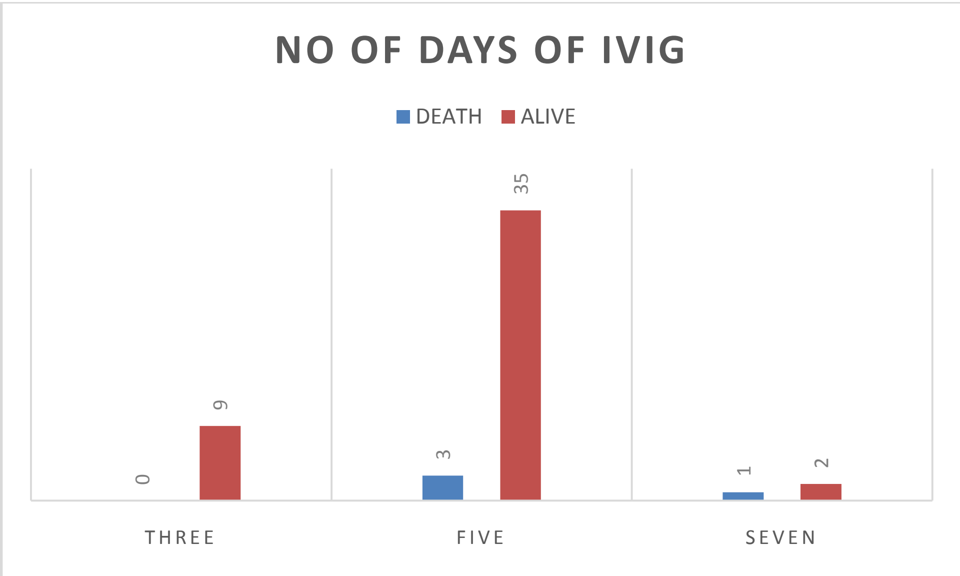


Table 32 : TYPE OF NEUROPATHY AND END POINT

	END POINT	
TYPE OF NEUROPATHY	**DEATH**	**ALIVE**
AMAN	3	2
AIDP	1	44
P VALUE - 0.001		
SIGNIFICANT		
CHI SQUARE TEST		

There is significant influence of type of neuropathy over final endpoint (Death) with p value of 0.001.AMAN has more chance of ending up in mortality.

Figure 32 : TYPE OF NEUROPATHY AND END POINT.

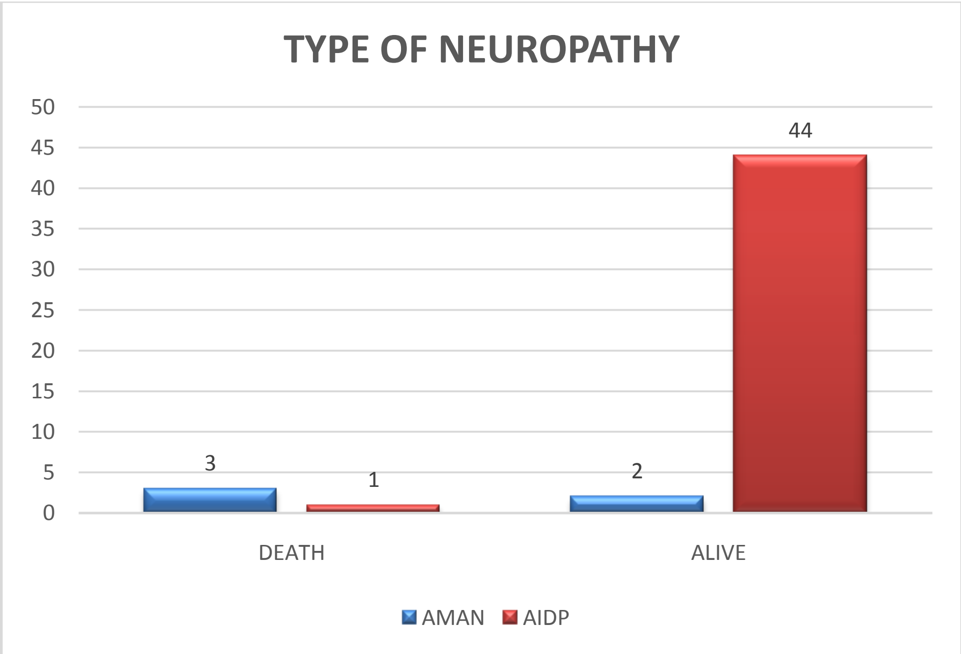


Table 33 : CRANIAL NERVE INVOLVEMENT AND END POINT

	END POINT	
CRANIAL NERVE INVOLVEMENT	**DEATH**	**ALIVE**
YES	3	12
NO	1	34
P VALUE - 0.041		
SIGNIFICANT		
CHI SQUARE TEST		

There is significant influence of cranial nerve involvement over final endpoint (Death) with p value of 0.041.

Figure 33 : CRANIAL NERVE INVOLVEMENT AND END POINT.

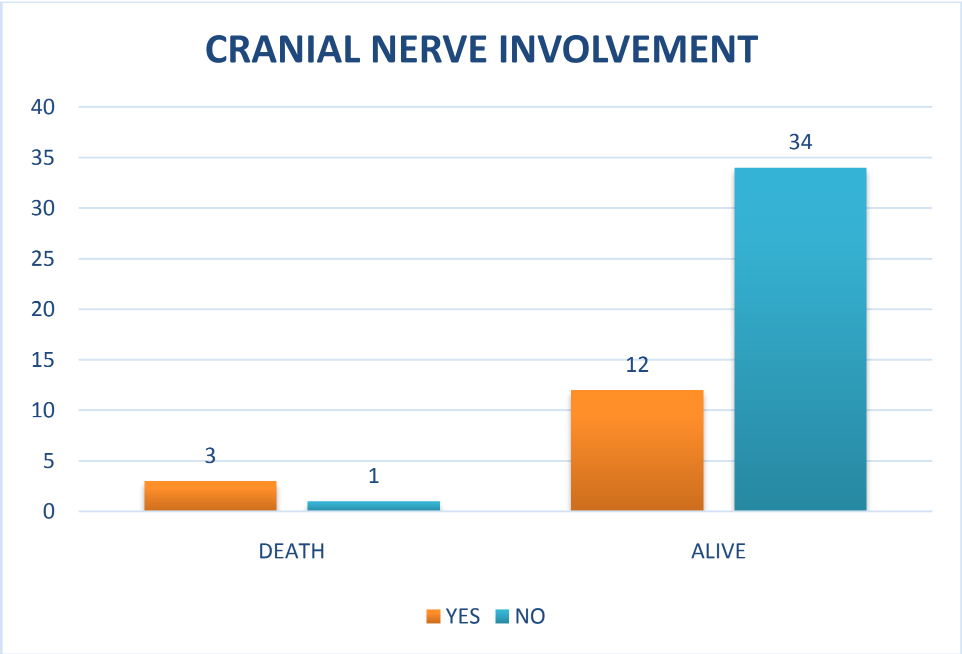
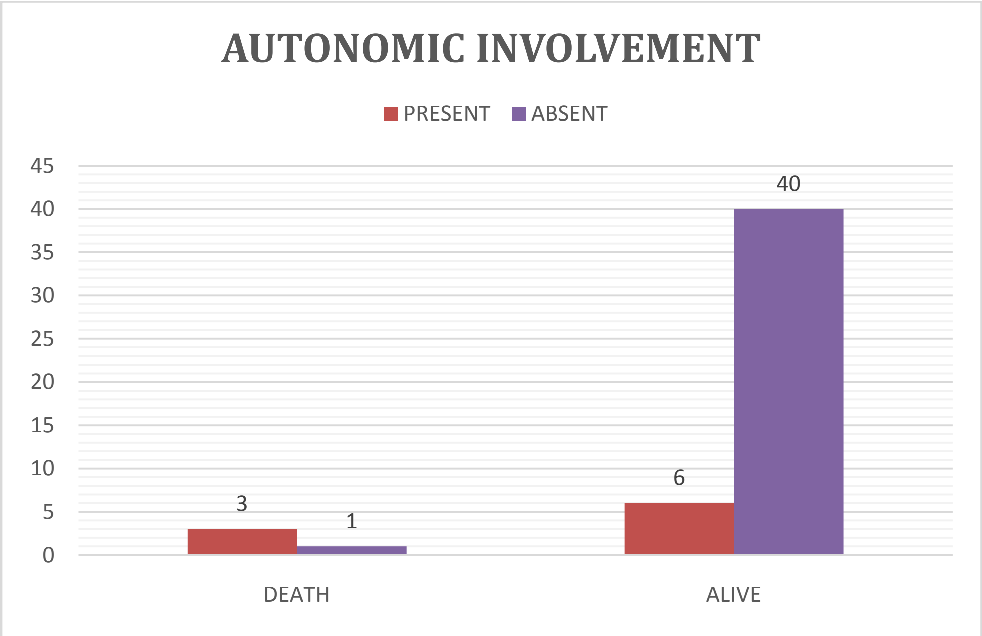


Table 34 : AUTONOMIC INVOLVEMENT AND END POINT

	END POINT	
AUTONOMIC INVOLVEMENT	**DEATH**	**ALIVE**
PRESENT	3	6
ABSENT	1	40
P VALUE - 0.002		
SIGNIFICANT		
CHI SQUARE TEST		

There is significant influence of autonomic involvement over final endpoint (Death) with p value of 0.002.

Figure 34 : AUTONOMIC INVOLVEMENT AND END POINT



DISCUSSION

DISCUSSION

Guillain- Barré syndrome (GBS) affects all ages, men more than women, with a lifetime risk of one in 1,000. [130] Overall incidence of GBS increases by 20% for every decade of life after 10 years of age, although some studies have shown an incidence drop after age 80 years. In our study there is more incidence in the age below 30 years, followed by 13 patients in the age group of 30-45 years ,and 12 between 45 to 60 years ,about 8 patients were in the age group above sixty years. From our study we can find that incidence is not present, only in the extreme ranges but its prevalant wide distributed. Age factor has no influence in acquiring the disease. Every age group has varied manifestations of the disease with different presentations. There is significant influence of age with patient’s age less than 30 have better improvement in power which is also statistically significant with p value of 0.009.

The subtypes of GBS have different incidence rates in different parts of the world. In Europe and North America AIDP is dominant contributing to 90% of the cases. In contrast in China and Japan AMAN being the most common subtype.[131][132] . In Indian series the incidence of AIDP and AMAN are virtually equal although AMAN is more common in younger patients.[133]There seems to be a slight preponderance of AIDP in studies by Gupta *et al*[134] and by Meena et al (unpublished data from NIMS, Hyderabad). In western countries, GBS is common in the 5th decade,[135] but in India it occurs more commonly at a younger age.[136][137] GBS is equally common in men and women and can occur at any age. There is a male preponderance among the hospitalized population.[136][137]. In our study also the male population presented more in number than the female sex.

Time of presentation to the hospital from the time of onset of symptoms plays a pivotal role in the course of disease, treatment and management of the illness. In our study 35 patients presented before 24 hours and 15 patients after 24 hours. First group had better outcome during the course of the treatment and at the time of discharge. There is significant influence of time interval between on set to admission with patients admitted before 24 hrs have better improvement in power which is also statistically significant with P value of 0.046.There is no significant influence of time of onset to admission over final endpoint (Death) with p value of 0.820

In our study patients with power of MRC SSS (0-19) was about 24 patients ,around 48 percent and 26 patients with MRC SSS (20-29) were 52 percent. After the course of treatment with IVIg for 3 to 5 days patient recovered with power at the end of discharge was 3 persons with MRC SSS (20-29), 18 persons with MRC SSS of (30-39),around 29 persons were with MRC SSS of power $\geq$ 40.There is no significant influence of mean no of days of IVIg over final endpoint (Death) with p value of 0.109.

Although IVIg versus placebo has never been studied in adults, 5 trials comparing IVIg to PE for GBS have been reported.[88][98][140] A recent meta-analysis of these studies found no difference between IVIg and PE in terms of improvement at 4 weeks, mortality, residual disability, or time for need of mechanical ventilation.[99]A single study found that IVIg added after PE offered a small, but statistically insignificant, benefit over IVIg alone.[26] The mechanism by which IVIg exerts its beneficial effect in GBS is not firmly established, but it may neutralize autoantibodies or cytokines, saturate macrophage Fc receptors, or inhibit complement activation.[141]

Good nursing care with Intravenous Immunoglobulins or plasmapheresis is considered as effective mode of treatment of GBS by many studies (Rostani A Metal, Ranfala H et al, RDM Hadden et al). IVIg is considered as treatment of choice in GBS in the dose of 400 mg/kg/day for five days by RDM Hadden et al.

The most common IVIg dose is 0.5 g/kg split evenly over 5 days, but the optimal dose and dosing regimen remains unknown. The only study addressing the amount of IVIg administered suggested a trend toward greater improvement with 6 days versus 3 days of therapy. [142]However, this study included only 39 patients and therefore definite conclusions could not be drawn. Recent data suggests that a “one-size fits all” approach to IVIg dosing may be inadequate. Kuitwaard et al measured total serum IgG 2 weeks after IVIg treatment, showing that patients whose IgG rose the least had worse outcomes at 6 months.[143] Whether this implies that additional doses of IVIg should be given to those with smaller treatment-related increases in serum IgG remains to be established.

Because studies have administered IVIg within 14 days of symptom onset, it is also unknown whether IVIg is effective after this time point. There is no evidence favoring one IVIg preparation/brand over another in the treatment of GBS. Sparse anecdotal data suggests that some patients treated with IVIg with "treatment-related fluctuations" receive further benefit from retreatment.[144]

Although IVIg is relatively safe to administer, adverse events occur in about 5% of patients and commonly include infusion-related headache, myalgias, chills, and nausea.[145] These are typically managed with symptomatic medications and by stopping the infusion temporarily before resuming at a slower rate. Aseptic meningitis is rarer complication and typically develops after the infusion is completed. Treatment often requires nonsteroidal anti-inflammatories and/or opiates.[146]Serious side-effects from IVIg are rare but include congestive heart failure, stroke, myocardial ischemia, renal failure, thrombocytopenia, hemolysis and anaphylactic shock. Slower infusion rates may prevent cardiac complications in patients with cardiac disease.[147] Risk of anaphylaxis appears greatest in patients with IgA deficiency and circulating antibodies against IgA. Checking qualitative IgA levels prior to administering IVIg will identify those at risk and permit the use of IgA-depleted formulations of IVIg or favor the use of PE. Because treatment with PE and IVIg are equally effective, the choice between them is dictated by treatment availability, facility expertise, and patient comorbidities or contraindications. The fact that most hospitals stock IVIg and have familiarity with its use has dramatically changed GBS treatment practices. For example, in the decade following the first IVIg study, rates of plasmapheresis in the United States plummeted from 24.5% to 14.7% of admissions, while the rate of IVIg usage increased by a reciprocal amount.[148] A similar great change in European treatment practices even forced the early termination of a GBS treatment trial in Germany.[149] In our study there is no significant influence mean no of days of requirement of IVIG over functional outcome (improvement in power). Among for group of 5 days course of IVIg 38 patients showed improvement in MRC SSS and with group of 3 days course of IVIg 9 patients showed improvement. In former group 7 patients showed improvement of MRC SSS (0to <60) and in the latter group only 2 were present.

Although corticosteroids are a highly effective therapy for chronic inflammatory demyelinating polyneuropathy (CIDP), they are generally avoided in GBS. Meta-analysis of relevant studies has shown no advantage of intravenous methylprednisolone and actually suggested less improvement in patients treated with oral corticosteroids.[150]

Respiratory failure is one of the most common serious complications of GBS, if unnoticed, can be life-threatening result with significant morbidity. As study done by RDM Hadden, RAC Hughes had 20 % of incidence, while Teitebaum J.S. et al had 10 to 30 % incidence.

In our study, the respiratory failure was observed in 15 patients with need for mechanical ventilation for around 9 patients due to low forced vital capacity. Among 9 patients with ventillatory support 4 were of AMAN type and 5 were of AIDP type. Morbidity due to ventillatory support was 3 patients in our study was very significant . There is significant influence of respiratory distress with there is better improvement in patient who doesn't has respiratory distress which is also statistically significant with p value of 0.040

Before mechanical ventilation, the mortality rate in GBS exceeded 30%, mostly from respiratory failure.[151] The percentage of patients with GBS ultimately requiring mechanical ventilation depends on study methodology (clinical trials versus population-based) but ranges from 25% to 44%.[77][91][94][152] Phrenic and intercostal nerve demyelination produce restrictive lung mechanics while bulbar muscle palsy may prevent adequate airway protection and puts patients at risk for aspiration.

The respiratory status of patients with GBS must therefore be carefully and frequently monitored. Pulse oximetry and blood gases are inadequate for early detection of failure because hypoxemia and hypercarbia are very late manifestations. Instead, regular bedside monitoring of the vital capacity, maximal inspiratory pressure (MIP or PImax), and maximal expiratory pressures (MEP or PEmax) should be used. Admission to an ICU is necessary if measured values fall below the "20/30/40 rule" that is, the VC falls below 20 mL/kg, MIP above −30 cm H_2O, or MEP below 40 cm H_20).[153] .Single breath count test is used to moniter the vital capacity.

The time for independent breathing can be delayed in GBS, resulting in prolonged periods of mechanical ventilation. One half of intubated patients with GBS ultimately require tracheostomy,[154] but the optimal timing of tracheostomy is debated. Delaying tracheostomy >14 days after intubation has been associated with a higher incidence of ventilator-associated pneumonia and longer duration of mechanical ventilation,[155] but earlier intervention will result in some patients getting an unnecessary tracheostomy. In our study we have done tracheostomy for 4 patients with significant morbidity around two due to aspiration.

The severity of autonomic involvement is not related to the degree of sensory and motor disturbance which is consistent with the patchy distribution of lesions throughout the peripheral and autonomic nervous systems.

Acute dysautonomia is a significant cause of death in patients with GBS. Cardiac and hemodynamic disturbance manifesting as hypertension, postural hypotension, and tachycardia occur in a majority of GBS patients. This is due to excessive sympathetic over activity and parasympathetic under activity. Severe dysautonomia occurs usually in severe cases at the peak of the deficit.[155] Tachycardia is most common, usually in the range of 100–120/min, which does not require treatment. Approach to inserting a pacemaker for serious bradycardia or sinus arrest has varied widely because of the uncertainty that exists in anticipating such events at the bed side by different ways. However, the presence of tachycardia, increased daily variation in systolic blood pressure, reduced normal respiratory-induced heart rate variation, and first episode of severe bradyarrhythmia reduce the threshold for insertion of pacemaker.[156][157]. Endotrachial suction may provoke bradycardia or systole, and this can be reduced by hyperoxygenation. Hypertension is seen in one third of patients with GBS and can be labile or be followed by hypotension.[159][160][161]. If hypertension is severe (mean pressure greater than approximately 125 mmHg) and sustained, specific therapy may be necessary. Antihypertensives with short half-lives (labetolol, esmolol, or nitroprusside infusions) should be considered.[161]. Beta-adrenergic or calcium channel blockers should be used with caution, especially if episodes of hypertension alternate with hypotension. Hypotension can be managed by maintaining intravascular volume and avoid using diuretics. Patients with a risk of hypotension should not be left unattended in a sitting or upright position. Pronounced and persistent hypotension should warrant search for other causes, such as sepsis myocardial infarction and pulmonary thromboembolism or use of narcotics or positive pressure ventilation. Gastrointestinal motility disorders occur in 15% of severely affected GBS patients. Ileus is associated with other features of dysautonomia (tachycardia and hypertension). Dysmotility can be effectively managed by suspension of enteral feeds, nasogastric suctioning, and erythromycin or neostigmine.[156].

In our study 9 patients had involvement of autonomic system, among them 3 died during the course of illness. Cause of morbidity was mainly due to hypotension , with abnormal sweating, ECG had no clues of infarction, patient had no history of Diabetes or previous history of ischemic heart disease. Even there was no evidence of sepsis from lab investigations done. The cause of death is mainly attributed to autonomic failure in spite of early detection and treatment. Other 6 patients with autonomic involvement had abnormal sweat rate, tachycardia, gastro-intestinal dysmotility. Constipation was a major compliant in almost all patients, so need of laxatives is certain for GBS patients.

Cranial nerve involvement is common in GBS , however there are no studies only focused on cranial nerve in GBS. Many of the physicians miss the cranial nerve involvement in clinical examination, until unless the patient complains about that, hence less number of cases are diagnosed up. If we are careful enough and look for cranial nerve involvement, the study yield will be large and better attention can be given accordingly. In our study 38 (62.3%) patients was seen with cranial nerve involvement. Most of the studies done before shows variable involvement of cranial nerves ranging from 50% to 75%, which correlates well with Lφeffel, *et al*. [162] have quoted 50% and Dhadke, *et al*. [163] had 62.5% involvement. Most of our patients (65%) had more than one cranial nerve involvement, suggesting a insult to the systemic component. Most of the patients with cranial nerve involvement as palsies had marked quadriparesis making them bed ridden, suggesting more severity of the illness in them.Certain patients didn't complain about symptomatology of cranial neuropathy, like in facial palsy out of 8 patients, 5 didn't complain. On examination they found be having bilateral facial palsy of mild to moderate severity. Hence, detailed history and examination is must to detect these cases

Bulbar palsy was the most common (49.2%) in our study, which correlates with so many studies till now reported. Among bulbar palsy patients majority had dysphagia and few had dysphonia. These patients were kept on Ryle's tube feeding, and in two patients it was an indication for intubation because of copious secretions. In the follow up of patients at end of 1 month all of them had complete recovery.

Facial palsy was seen in 8 (46%) patients, all had bilateral involvement except 3, who had unilateral palsy. In many of the studies facial palsy was the most common finding with percentage ranging from 45% to 53%. In a study by Winer, *et al*.[164] 53% had bilateral facial palsy. In our patients three had unilateral palsy, which is rare but many case reports are there in the literature with unilateral palsy (Kamihiro, *et al*. and Verma, *et al*).[165][166]. Only four patients complained about altered taste sensation, suggesting proximal involvement of facial nerve. At 1 month of follow up, 15 patients had partial recovery and rest had complete recovery. At the end of 2 months remaining 15 patients also had complete recovery.

Ophthalmoplegia was seen in 3 of our patients, which was similar to findings noted by Winer, *et al*.[164] Deafness was seen in one patient, in whom audiogram revealed sensoryneural hearing loss in both ears. Although it's a rare finding, there are few case reports describing this entity (Takazawa, *et al*.)[167]. In patients of ophthalmoplegia, their main complaint was diplopia in whom two had complete external ophthalmoplegia and remaining one had partial ophthalmoplegia. All these patients had multiple cranial nerve palsies including facial and bulbar palsies. Most of these patients recovered completely over 1 to 2 months.

On comparing various parameters among patients of GBS with cranial nerve involvement significant association was seen with respiratory paralysis, IVIg requirement and ventilator support among patients with cranial nerve palsies. Other parameters didn’t show any correlation, suggesting age, sex, antecedent illness are not related to the presence or absence of cranial nerve palsies. In our study AMAN Subtypes of GBS had cranial nerve involvement with bulbar palsy. Majority of bulbar palsy involved patients had respiratory paralysis, suggesting an indicator of respiratory involvement as mentioned in earlier studies. Recovery of cranial nerve palsies is earlier as compared to motor deficits.

In our study we found some rare cranial nerve involvement, like involvement of vestibulocochlear in one patient, ophthalmoplegia in three patients. Time and again our study want to emphasis that careful clinical examination should be done to detect these rare entities.

At the end of 1 month follow up, 75% were able to walk unassisted and only 25% were needing support to walk or dependent for their activities of daily living. A large prospective study by van Koningsveld, *et al*.[108] had almost similar results, 82% of their patients were able to walk independently at the end of 6 months. In our study also there is no significant influence of cranial nerve involvement on power outcome.

According to study done by Winner Hughes et al in more than 50 % of cases there is a significant history of preceding illness. In the our study out of 50 patients twelve patients had history of preceding illness

The electrophysiologic evaluation of a suspected case of GBS remains a key extension of the clinical examination. Standard parameters of the motor nerve include the distal motor latencies, CMAP amplitudes, conduction velocities, waveform duration and morphology and F waves. Sensory nerve action potentials is the electrophysiologic correlate for the sensory nerve. The findings may be quite variable and beyond the nuances of GBS variants, and are often a function of the time during the disease course that the patient is evaluated. The hallmark of the classic GBS variant of AIDP rests in the basic pathophysiology of demyelination with occasional or variable secondary axonal degeneration. These patients exhibit prolonged distal latencies, slow conduction velocities, temporal dispersion, conduction block and prolonged F waves. At least three motor and sensory nerves with multi-site stimulation F waves and bilateral tibial H reflexes should be assessed on nerve conduction testing. Hughes and Cornblath outlined the electrophysiologic classification of GBS [67]. In that criterion, at least one of the defined markers of demyelination should be observed in each of at least two nerves. The entity of conduction block represents loss of myelin with neural conduction failure, which may lead to acute weakness and sensory loss. It is embodied in > 20% reduction in baseline to peak CMAP from proximal to distal stimulation sites. Conduction block may be seen in 74% of patients with AIDP within the first two weeks of their disease course. Approximately 40−60% of AIDP patients eventually demonstrate SNAP amplitude reduction or absence by the third or fourth week of the illness. This may be attributable to conduction block or secondary axonal degeneration.

In our study there were 5 patients of AMAN type diagnosed electrophysiologically, among them 4 died due to severe illness with complications . Bulbar palsy with dysphonia was seen in one patient who was on ventillatory support for more than one month inspite of two cycles of 5 days of IVIg, but had no improvement. Its not certain that axonal variant respond very slow to IVIg inspite of early treatment. One patient of AMAN recovered well with ventilatory support and IVig therapy inspite of bulbar palsy with respiratory distress .Many studies show that AMAN subtype has poor prognosis.It is possible that several different pathophysiological processes exist in AMAN to explain the dichotomous recovery patterns: reversible distal nerve failure at motor terminals or conduction block at nodes of Ranvier in association with rapid recovery, and Wallerian degeneration requiring axonal regrowth which may continue over many months and years. In AIDP, conventionally considered a demyelinating condition, severe lesions may result in axonal degeneration as well as myelin destruction, and a similar distinction dependent on disease severity may occur in AMAN. Certainly there is no unifying hypothesis to date, but it is encouraging that all forms seem to be potentially reversible.

Rapid recovery in AMAN in the current study was defined as an improvement of two or more Guillain–Barré syndrome disability scale grades in the first four weeks e.g. from bed-bound to independent ambulation. Such improvement would be incompatible with the primary pathology being Wallerian degeneration. Other explanations might be degeneration restricted to the distal motor nerve terminal where regeneration could occur quickly, immune mediated conduction block at the axonal membrane, or complement mediated damage to perisynaptic Schwann cells. This may imply additional pathological mechanisms distinct from those described ultrastructurally by Griffin and colleagues. The authors also identified a small number of patients who were unable to walk six months after the illness but all of whom continued to improve until they could walk independently in subsequent years.

CONCLUSION

CONCLUSION

Our study has varied age and sex of presentation, the incidence of male population was more as similar to other study group. The time of onset of symptoms to admission to hospital with less than 24 hours and more than 24 hours had no significance over the mortality in the end. But early presentations to the hospital had better improvement in the power.

The days of administration of IVIg for 3 and 5 days had no significant outcome in the mortality of the patients.

For patients without respiratory distress and mechanical ventilation had better outcome in prognosis than with the support of it.

Further involvement of autonomic system should be diagnosed early to prevent morbidity which does not influence the motor system involvement and its prognosis.

Cranial nerve involvement should be clinically diagnosed at the time of admission to prevent further deterioration in the course of illness and to earlier assessment for need of ventilator support.

Electrophysiological diagnosis of the cases to delineate the sub types of GBS plays a pivotal role for supportive care and in-depth management of AMAN type of GBS.

Our study brings out various predictors in GBS patients still certain predictors has more morbidity and poor outcome. Although many predictors are involved in the survival of the patients, careful clinical examination and electrophysiology with intense treatment and supportive care may help in preventing the mortality rate in GBS and achieving good prognosis.

SUMMARY

SUMMARY

- 50 patients with GBS were admitted to Coimbatore Medical College Hospital between -July 2016 – July 2017 were included in the study.
- Commonest age group involved below 30 years.
- Males are the most common to present with GBS.
- Majority of patients were presented less than 24 hours from onset of symptoms to admission.
- 52% had MRC SUM SCORE of 20-29 at admission
- 63% had MRC SUM SCORE of $\geq$ 40 at discharge.
- 15 Patients had respiratory difficulty at time of presentation among them 9 needed ventillatory support .
- 38 patients were given IVIg for 5 days, 3 patients for 7 days , 9 patients for 3 days.
- AIDP were present in 45 patients and AMAN were present in 5 patients.
- Cranial Nerve involvement were present in 15 patients.
- Autonomic involvement in 9 patients.
- Total dead in the end point , among the study group was 4.
- 18% had improvement of power MRC SUM SCORE between 10-60.
- 40% had improvement of power MRC SUM SCORE between 20-60.
- There is significant influence of age with patient's age less than 30 have better improvement in power.

- There is significant influence of time interval between onset to admission with patients admitted before 24 hrs have better improvement in power.
- There is significant influence of respiratory distress with there is better improvement in patient who doesn't has respiratory distress .
- There is significant influence of ventilator support with there is better improvement in patient who doesn't end up in requiring ventilator support.
- There is no significant influence of no of days of IVIG over improvement of power. There is no significant influence mean no of days of requirement of IVIg over functional outcome.
- There is significant influence of type of neuropathy with patient's with AIDP have better improvement. There was better improvement of power in patients with autonomic involvement.
- There is no significant influence of age over final endpoint (Death). There is no significant influence of time of onset to admission over final endpoint.
- Patients who end up in mortality have more chance of respiratory difficulty. Patient having more chance of mortality require ventilator support.
- There is no significant influence of mean no of days of IVIg over final endpoint. AMAN has more chance of ending up in mortality.
- There is significant influence of cranial nerve involvement over final endpoint (Death).
- There is significant influence of autonomic involvement over final endpoint (Death)

LIMITATIONS

LIMITATIONS

Our study involves very small group of patients which makes a set back in analysis of various manifestations of predictors.

Also complications of various predictors could not be studied with in depth data due to less population group.

Our study group had only with treatment of IVIg, but other studies has better outcome with plasmapheresis. Further in some studies both were used simultaneously the results of it had varied outcome.

Our study does not involved with measuring of antibodies associated with GBS, it might have been useful to prediction various subtypes of GBS further adding more evidence to it.

We have measured outcomes with available treatment and investigations in our set up.

RECOMMENDATIONS

RECOMMENDATIONS

Number of Study population should be large to give more evidence of predictors for its morbidity and mortality.

Use of both plasmapheresis and IVIg should be analysed in selective group of patients with late presentation ,other subtypes of GBS like AMSAN ,AMAN.

Need to establish separate unit as intensive neuro critical care for GBS and special out patient department unit to assess the outcome of patients for longer periods upto many years to find out any relapses such as to identify Chronic inflammatory Demyelinating Polyneuropathy.

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ANNEXURES

ANNEXURE-1

PROFORMA

NAME		AGE	
OCCUPATION		SEX	
SOCIO ECONOMIC STATUS		IP NO	
ADDRESS AND CONTACT NO			
CHIEF COMPLAINTS			
PRESENT HISTORY 1. WEAKNESS OF UPPER LIMB 2. WEAKNESS OF LOWER LIMB 3. DIFFICULTY IN SWALLOWING 4. DIFFICULTY IN CHEWING 5. DIFFICULTY IN VISION 6. DYSPNEA 7. SENSORY DISTURBUNCE 8. BLADDER DISTURBUNCE 9. PALPITATION 10. GIDDINESS 11. SWEATING 12. ABDOMINAL DISTENSION	Yes/no	Duration	Other features

<table>
<tr><td>13. OTHER SPECIFIC COMPLIANTS</td><td></td><td></td><td></td></tr>
<tr><td>PAST HISTORY
1. SHT
2. DM
3. CAD
4. TB
5. EPILEPSY/CVA
6. LIVER DISEASES
7. SIMILAR HISTORY IN PAST</td><td>Duration</td><td colspan="2">Treatment</td></tr>
<tr><td>PERSONAL HISTORY
1. ALCOHOL CONSUMPTION-
2. SMOKING
3. DIET
4. DRUG INTAKE</td><td colspan="3">Quantity - Duration</td></tr>
<tr><td>GENERAL EXAMINATION
BP
PR
SPO2
TEMP
RR</td><td colspan="3">CONSCIOUS LEVEL-
PALLOR
ICTERUS-
CYANOSIS-
DYSPNEA-
PEDAL EDEMA-
SINGLE BREATH COUNT-</td></tr>
<tr><td>SYSTEM EXAMINATION –</td><td colspan="3"></td></tr>
<tr><td>CVS</td><td colspan="3"></td></tr>
<tr><td>RS</td><td colspan="3"></td></tr>
<tr><td>ABD</td><td colspan="3"></td></tr>
</table>

CNS EXAMINATION

DAYS OF HOSPITAL STAY	TONE		POWER		REFLEXES		NECK FLOP RESP DIFFICULT	CRANIAL NERVE INVOLVE MENT	SENSORY INVOLVE MENT	MRC SSS	TRE ATM ENT
	UL	LL	UL	LL	UL	LL					

BASE LINE INVESTIGATIONS-	CBC PERIPHERAL SMEAR	RFT &RBS	LFT
SPECIAL INVESTIGATIONS	CSF ANALYSIS	HBsAg	Anti HCV HIV 1 AND 2
INVESTIGATIONS	USG	CHEST X-RAY	ECG
CSF ALBUMINO CYTOLOGICAL DISSOCIATION YES /NO		ESR	C-REACTIVE PROTEIN
NCS	AIDP		
	AMAN		
	AMSAN		
	MFS		
	OTHERS		
FINAL DIAGNOSIS			

ANNEXURE -2

CONSENT FORM

Yourself Mr./Mrs./Ms………………………………..are being asked to be a participant in the research study titled "A study of Prognostic Predictors in Guillain-Barré syndrome"in Coimbatore Medical College Hospital, Coimbatore, conducted by DR.SHAKTHI RAJA GURU .G M.D., Post Graduate Student, Department of General Medicine, Coimbatore Medical College. You are eligible after looking into the inclusion criteria. You can ask any question you may have before agreeing to participate.

Research Being Done

A study of prognostic predictors of Guillain-Barre Syndrome

Purpose of Research

- To study clinical and investigative profile of patients with Guillain Barre Syndrome.
- To study the prognostic predictors of GBS with various predictors and its functional outcome.

Decline from Participation

You have the option to decline from participation in the study existing protocol for your condition.

Privacy and Confidentiality

Privacy of individuals will be respected and any information about you or provided by you during the study will be kept strictly confidential.

Authorization to publish Results

Results of the study may be published for scientific purposes and/or presented to scientific groups, however you will not be identified.

Statement of Consent

I volunteer and consent to participate in this study. I have read the consent or it has been read to me. The study has been fully explained to me, and I may ask questions at any time.

------------------------------- -------------------------------

Signature /Left thumb impression Date

(volunteer)

-------------------------------- --------------------------------

Signature of witness Date

-------------------------------- --------------------------------

Signature of Guardian Date

ஒப்புதல் படிவம்

பெயர் :

வயது :

பாலினம் :

முகவரி :

கோவை அரசு மருத்துவக் கல்லூரி மருத்துவமனையில் மருத்துவர் சக்தி ராஜ குரு.கோ தலைமையில் நடைபெறும் இந்த ஆய்வில் முழு சம்மதத்துடன் கலந்து கொள்ள சம்மதிக்கிறேன். இந்த ஆய்வில் என்னை பற்றி விவரங்களை பாதுகாப்புடன் இந்த ஆய்வில் வெளியிட ஆட்சேபனை இல்லை என்று தெரிவித்துக் கொள்கிறேன். எந்த நேரத்திலும் ஆய்வில் இருந்து எந்த நேரத்திலும் விலக்கிக் கொள்ளும் உரிமை உண்டு என்று அறிவேன்.

இடம் :

தேதி :

கையொப்பம் / ரேகை

ANNEXURE – 3
MASTER CHART

S. No	name	age	sex	time from onset to IVIg	power at admission	power at 1 discharge	respiratory difficulty at admission	ventilatory support	no.of days IVIG given	autonomic symptoms	cranial involvement	neuropathy type	death
1	pushpam	62	2	1	2	3	2	2	3	2	2	1	2
2	dilip khan	45	1	1	1	3	2	2	3	2	2	1	2
3	sivakumar	17	1	1	2	4	1	2	5	2	2	1	2
4	anguraj	40	1	1	2	4	2	2	5	2	2	1	2
5	mahendran	22	1	2	1	3	1	2	3	2	2	1	2
6	thirupathy	41	1	2	2	4	1	2	5	2	1	1	2
7	thirumoorthy	41	1	1	1	3	2	2	5	1	2	2	2
8	radha	48	2	1	2	4	2	1	5	2	1	1	2
9	aravind	15	1	1	1	4	1	1	5	2	2	1	2
10	kalaivani	28	2	2	2	4	2	2	5	1	2	1	2
11	sarasu	55	2	2	2	4	2	2	3	2	1	1	2
12	karupusamy	80	1	1	1	3	1	1	5	2	1	1	2
13	sherif	14	1	1	2	4	2	2	5	2	1	1	2
14	ramasamy	70	1	1	1	2	1	1	5	1	1	2	1
15	subramanium	65	1	1	1	3	1	2	5	2	1	1	2
16	sangeetha	15	2	1	2	4	2	2	3	2	2	1	2
17	selvaraj	52	1	2	2	3	2	2	5	1	2	1	2
18	krishnan	62	1	1	1	4	2	2	5	2	2	1	2

S. No	name	age	sex	time from onset to IVIg	power at admission	power at 1 discharge	respiratory difficulty at admission	ventilatory support	no.of days IVIG given	autonomic symptoms	cranial involvement	neuropathy type	death
19	sasikala	29	2	1	2	4	2	2	5	2	1	1	2
20	jayasri	16	2	1	1	4	2	2	5	1	2	1	2
21	syedullah	52	2	2	1	4	2	2	5	1	2	1	2
22	sunderasa ganesan	60	1	1	2	3	2	2	5	2	2	1	2
23	krishnan s	56	1	2	1	3	2	2	5	2	2	1	2
24	rubeena	36	2	2	2	4	1	1	5	2	1	1	2
25	mobeena	35	2	2	1	3	2	2	5	2	1	1	2
26	revathy	14	2	2	1	3	2	2	5	2	2	1	2
27	velusamy	38	1	1	1	2	1	1	5	1	1	2	1
28	palanisamy	60	1	1	2	3	1	2	5	2	2	1	2
29	chandrakala	32	2	2	1	3	2	2	5	2	2	1	2
30	dhanalakshmi	41	2	2	2	4	1	2	5	2	2	1	2
31	krishnan s	62	1	2	1	2	1	1	5	2	2	1	1
32	balaji	47	1	1	1	4	2	2	3	2	2	1	2
33	latha	42	2	1	1	3	2	2	3	2	2	1	2
34	sekhar	46	1	1	2	4	2	2	5	1	2	1	2
35	rajesh	26	1	1	1	4	2	2	5	2	2	1	2
36	andrews	57	1	1	2	3	1	1	7	2	1	2	2
37	perumal	27	1	1	1	4	2	2	5	2	2	1	2
38	radhika	31	2	1	2	4	2	2	5	2	2	1	2

S. No	name	age	sex	time from onset to IVIg	power at admission	power at 1 discharge	respiratory difficulty at admission	ventilatory support	no.of days IVIG given	autonomic symptoms	cranial involvement	neuropathy type	death
39	kavitha	20	2	1	1	3	2	2	5	2	1	1	2
40	vigneshwaran	14	1	1	2	4	2	2	5	2	1	1	2
41	usha	47	1	1	2	3	1	1	7	2	1	2	1
42	sangeetha	19	2	2	2	4	2	2	5	2	2	1	2
43	babu	27	1	1	1	3	2	2	7	2	2	1	2
44	nandhini	25	1	1	1	4	2	2	5	2	2	1	2
45	narmadha	22	2	1	2	4	2	2	5	2	2	1	2
46	kadhirvel	37	1	1	1	4	2	2	3	2	2	1	2
47	karuppan	53	2	1	2	4	2	2	5	2	2	1	2
48	balamurugan	64	1	2	2	4	1	2	5	2	2	1	2
49	priya	16	2	1	2	4	2	2	3	2	2	1	2
50	devi	35	2	1	2	4	2	2	5	2	2	1	2

age	n= Number in years	
sex	1 = male	2= female
time from onset to IVIg	1=<24hrs	2=>24hrs
power at admission	n = Number	
power at discharge	n = Number	
respiratory difficulty at admission	1= yes	2 = no
ventilatory support	1= yes	2= no
no.of days IVIg given		
cranial involvement	1 = yes	2 = no
neuropathy type	1 = AIDP	2 = AMAN
death	1 = yes	2 = no